DERMALA inc

The Human Microbiome Company

Spinout from UC San Diego

JLABS Incubator Company

Business Plan

2016 InnovateHER

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Dermala Inc. - Business Plan

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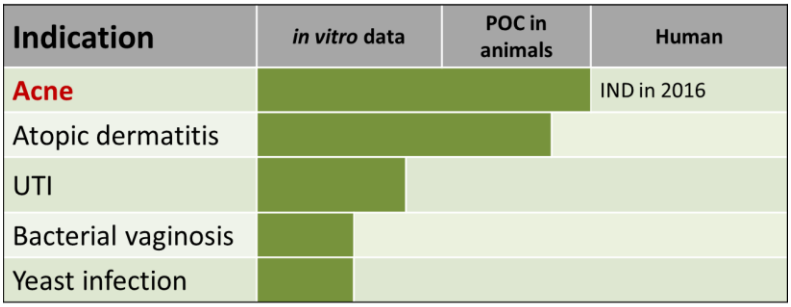
Executive Summary

Our goal is to provide safe, effective, and cost competitive solutions for unmet medical needs.

Technology. Trillions of microorganisms live on and in human bodies, collectively comprising the human microbiome. Dermala Inc., a 2014 spinout from the University of California San Diego, is using the human microbiome to develop novel solutions for unmet medical needs that are safe, effective, and cost competitive. Dermala's technology consist of sequencing the skin microbiome to characterize and diagnose the microbiome dysbiosis followed up by screening the human microbiome and metabolome to identify beneficial microbes and their metabolites that can be used to correct the dysbiosis and restore health. Dermala has demonstrated that commensal bacteria in the human microbiome can be used to combat various diseases and identified specific metabolites secreted by bacteria that have antibacterial and anti-inflammatory properties. Formulations derived from the commensal bacteria and their metabolites have favorable safety profiles, lower risk of generating resistance (vs. antibiotics), and require no immune responses to be effective (vs. vaccines).

Impact. Dermala's products will have a significant positive impact on the health of women and children.



Product Pipeline. Dermala's product pipeline includes candidates for the treatment and prevention of acne vulgaris, vaginal yeast infection, bacterial vaginosis, urinary tract infection and atopic dermatitis. The acne candidate is ready to enter clinical trials in 2016.

Market. Dermala is developing multibillion dollars market opportunities. Acne is the most common skin disease that affects adolescents and older women. Bacterial vaginosis and vaginal yeast infection are the two most prevalent vaginal infections in women of reproductive age. Urinary tract infection is the most frequent bacterial infection in women. Atopic dermatitis represents a global public health concern that is most common in infants. Global acne market is valued at $7B. Global candidiasis and bacterial vaginosis markets are estimated at $2 billion each. Urinary tract infection market is valued at $1.6B. Atopic dermatitis market is valued at $4B.

Team. Dermala's team has experience in drug development, microbiology/microbiome/metabolome, dermatology, bioinformatics, and business development. Dermala's advisors include Neal Matheson, the former CTO of Johnson & Johnson Family Consumer Companies, renowned clinical dermatologists, and microbiome and metabolome experts.

Company. Dermala is a Delaware C-corporation. The company is located at JLABS in San Diego, an incubator of Johnson & Johnson Innovation. Dermala has a worldwide exclusive license from the University of California and continues to strengthen its IP position through additional patent filings.

Funding. Dermala's product development is funded by angel investments and venture capital. The company is currently raising funds to support clinical development of the lead candidate for the treatment of acne.

Company Description

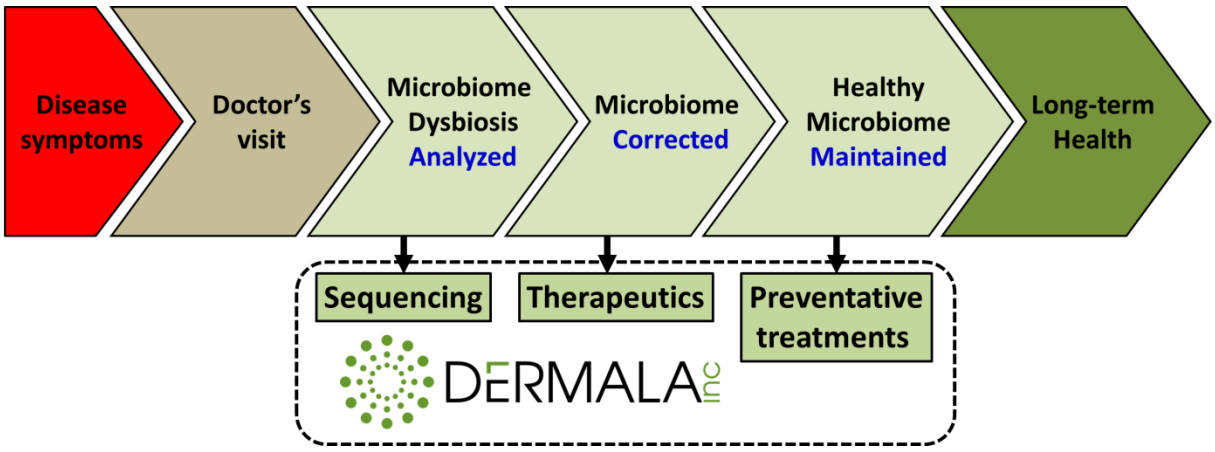
Dermala Inc. is a spinout from the University of California San Diego. The company was incorporated in 2014 and is located at JLABS, Johnson & Johnson Innovation incubator in San Diego.

Dermala is a pre-clinical stage biotechnology startup company that focuses on chronic diseases associated with defects (dysbiosis, imbalance) in the human microbiome. The human microbiome is a collection of microbes residing in and on human bodies. There are ten times more microbial cells than human cells and hundred times more microbial genes than human genes in and on a human body. The human microbiome plays an important role in keeping humans healthy. For example, in healthy individuals the microbiota provide a wide range of metabolic functions that humans lack. Defects (dysbiosis, imbalance) in the human microbiome often exhibits itself as a disease.

Dermala utilizes the human microbiome to identify and develop novel treatments for various diseases associated with defects in the human microbiome including chronic skin diseases (acne, atopic dermatitis) and chronic diseases affecting women (bacterial vaginosis, yeast infections, urinary tract infection), are recurrent and for which the current solutions do not meet the needs. Current treatments for these diseases have either significant side effects or limited efficacy. They do not prevent disease recurrence. They are also associated with is a growing problem of antibiotic resistance. There is a need to develop new therapeutic approaches and new therapeutic and preventative treatments for chronic skin diseases and diseases affecting women's health. These market segments represent multibillion-dollar opportunities with tremendous impact on improving the life of women worldwide.

Dermala's technology (Figure 1) consist of sequencing the microbiome to characterize and properly diagnose the dysbiosis in the microbiome followed up by screening the microbiome and metabolome to identify beneficial microbes and their metabolites that have a potential to correct the dysbiosis and restore health. Dermala's goal is to develop microbiome-based therapies for chronic diseases that incorporate microbiome sequencing and microbiome derived therapies into the treatment and prevention process.

Figure 1. Dermala's microbiome-based therapy



Dermala has multiple products in its pipeline (see Figure 2) in various stages of preclinical development, from *in vitro* identification of therapeutic candidates to pre-clinical validation in animal models, toxicology and safety studies, and IND enabling studies.

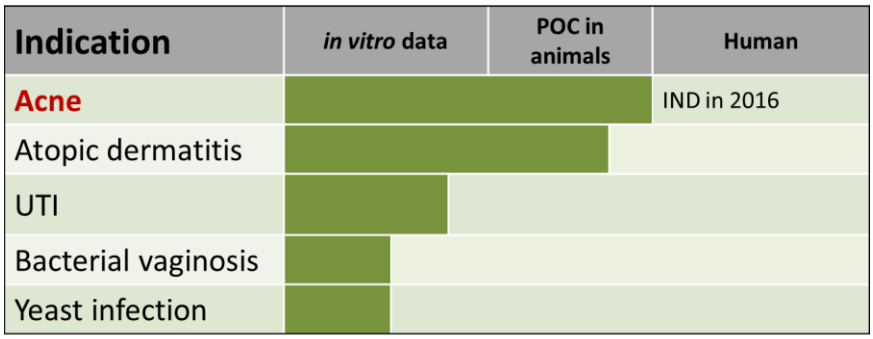


Figure 2. Product pipeline

Dermala's lead product candidate is for acne vulgaris. The lead molecule for acne shows suppression of *Propionibacterium acnes* (bacterium associated with acne) as well as reduction of Th1 acne associated inflammation in mice. The lead compound has favorable stability as well as safety profile (acute toxicity, subchronic/repeated dose toxicity, developmental and reproductive toxicity, carcinogenicity, genotoxicity). In addition, the compound has demonstrated no skin irritation or sensitization, which makes it superior to benzoyl peroxide. Benzoyl peroxide is the most common acne treatment in the US and the skin irritation is the most common reason for treatment non-compliance.

Candidates for urinary tract infection (UTI), bacterial vaginosis, and yeast infection show promising results *in vitro*. Urinary tract infection, bacterial vaginosis, and yeast infection are the most common, recurrent infections in women of reproductive age. These infections are currently treated with antibiotics and antifungals but an increase in resistance development is becoming an alarming problem. Developing new effective therapies is a critical need. The lead candidate for the prevention and/or treatment of atopic dermatitis (atopic eczema) shows suppression of *Staphylococcus aureus* (bacterium associated with atopic dermatitis) growth, prevention of *S. aureus* overgrowth and acceleration of skin healing in mice. There is no known cure or effective treatment for atopic dermatitis and the candidate under development by Dermala represents a novel promising therapy.

Dermala's competitive advantages include location, expert personnel, efficient operations, and ability to bring value to customers. Dermala is located at JLABS in San Diego, the Johnson & Johnson Innovation's "no strings attached" incubator. The incubator provides access to equipment, lab facilities, and expertise. Dermala has substantial intellectual property portfolio that provides a significant competitive advantage to the company. Dermala is utilizing human microbiome technology developed at the University of California San Diego (UCSD). Dermala has licensed this technology from the Regents of the University of California. Dermala has worldwide exclusive license for the use of the technology. Dermala continues to strengthen its IP position. Dermala's team has experience in drug development, microbiology/ microbiome/metabolome, dermatology, bioinformatics, and business development. Dermala's advisors include Neal Matheson, the former CTO of Johnson & Johnson Family Consumer Companies, renowned clinical dermatologists, and microbiome and metabolome experts.

Organization & Management

Dermala Inc.is a C-corporation incorporated in Delaware (operating in California).

Organizational Structure (see Figure 3)

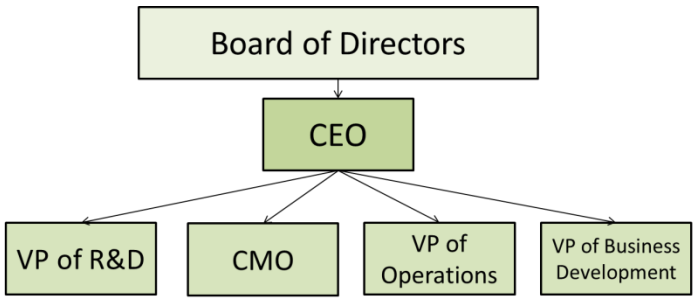


Figure 3. Organizational Chart

Dermala is an early stage biotechnology company. The company is deploying a pharmaceutical drug development approach that utilizes outsourcing to complete necessary product development steps fast, under reduced cost and with minimal capital expenditure.

The company organizational structure includes a board of directors, CEO, VP of R&D who directs pre-clinical research and development, chief medical officer who will direct clinical trials, VP of Operations who oversees company operations and VP of Business Development who oversees partnerships, licensing, and business development activities. The company performs preclinical research "in-house" in the JLABS incubator and partners and outsources majority of preclinical research and development, including animal studies, medicinal chemistry, analytical development, formulations, and manufacturing to CROs and other organizations with expertise in specific areas.

CEO

Lada Rasochova, PhD, MBA

Dr. Lada Rasochova is the co-founder, chief executive director and president of Dermala Inc., an early stage biotechnology company that uses the human microbiome to develop treatments for chronic skin diseases. Dr. Rasochova co-founded Dermala Inc. in 2014 based on a technology licensed from the UC San Diego.

Dr. Rasochova has been involved in commercialization of pharmaceutical and biotechnology products for the past 20 years. She spent more than 15 years in private sector where she held various leadership and management positions, most recently as the R&D Leader and Director of New Business Development in Dowpharma division of the Dow Chemical Company. In Dowpharma, she built and managed the Human Vaccine Division and advanced several vaccine candidates into human clinical trials. Prior to Dow, she was with Mycogen, a San Diego biotechnology startup that was acquired by Dow Chemical in 1998.

Dr. Rasochova joined the University of California in 2008 as the faculty member at the Rady School of Management to lead science and technology commercialization initiative at UC San Diego. She co-founded the California Institute for Innovation and Development (CIID) where she serves as the executive director, started the Rady Venture Fund where she is the managing director, and co-founded two award-winning startup accelerators, StartR and mystartupXX. CIID serves as a hub for commercialization of new technologies discoveries at UC San Diego. Rady Venture Fund Fund is a UC San Diego venture capital fund that makes investments in early stage technology ventures. StartR accelerator provides mentoring and support to early stage companies started by UC San Diego students and alumni. MystartupXX is one-of-its-kind accelerator that was created to increase and encourage diversity in entrepreneurship and

support the next generation of female founders of technology startups. Dr. Rasochova is the advisory board member for the Center for Drug Discovery Innovation and the Center for Center for Aerosol Impacts on Climate and the Environment at UC San Diego a and serves as a mentor for UC Regents Scholars Research Initiative**.** Dr. Rasochova teaches graduate level courses in Technology Commercialization and Venture Capital Management and serves as an advisor and board member of several startup companies.

Dr. Rasochova received her Ph.D. in molecular, cellular, and developmental biology from the Iowa State University and MBA from the Rady School of Management at UC San Diego. She did her postdoctoral studies at the University of Wisconsin-Madison. She is an inventor of several issued patents, authored many scientific publications, and received numerous national and international awards.

VP of R&D

Farah Babakhani, PhD

Dermala is also utilizing a consultant Simon Bailey, PhD who provides medicinal chemistry support.

VP of Operations

Michelle Kem, PhD

Dermala is also utilizing a consultant Ms. Silvia Chang who provides project management support.

CMO

To be hired.

Timeline: Before Dermala enters into clinical trials. At present, Dermala is utilizing a Regulatory Affairs consultant, Ms. Maggie Eras.

VP of Business Development

To be hired.

Timeline: After Dermala enters into clinical trials. At present, this function is provided by a consultant, Ms. Ann Derren Lewis.

Strategic Advisory Board

Neal Matheson

Neal Matheson is the former Chief Technology Officer (CTO) for the Johnson & Johnson Family of Consumer Companies, a role he held previously from 1994–2007. Neal returned to J&J in July 2012, where he helped to map the path forward for the global RD&E function as it embarked on a new course to drive growth and high-value innovation.

Between 2007 and his return to the J&J Consumer Group, Neal was based in London as CTO and Head of the New Business Unit at Unilever . His primary focus was to deliver new technologies to accelerate growth. While at Unilever, Neal reorganized the Discover part of R&D with a clear focus on breakthrough technology development, with transfer processes to Category Design teams. He was also responsible for identifying and progressing new business opportunities for the New Business Board, and he was accountable for the open innovation and patent and other critical functional capabilities.

Prior to Unilever, Neal spent 13 years as CTO for the J&J Consumer Group, where he helped achieve consistent above-market innovation driven growth. In particular, his contributions helped grow the Skin Care category from a relatively small business into a multi-billion dollar leader. Neal was also responsible for the Baby, Women's Health, Oral Care, Wound Care and OTC categories, as well as for professional Skin Care, Engineering and Quality Assurance.

Neal began his career at Procter & Gamble, where he spent more than 20 years and led R&D for many categories. Neal became P&G's first R&D leader for Beauty Care, laying the technical foundations for the vibrant growth of the Hair Care and Skin Care categories.

Throughout his career, Neal has been a champion of not only innovation to drive share growth but also people/ leadership development, taking pride in mentoring people to achieve career aspirations. Neal received his degree in Chemical Engineering from Queen's University.

Eric Huang PhD
Dr. Eric Huang is Professor of Dermatology at UC San Diego. He is the technology inventor, co-founder of Dermala and a strategic advisor to the company.

Other Advisors

Prof. Rob Knight, PhD – UC San Diego, world renowned expert on human microbiome
Prof. Joe Petrosino, PhD – Baylor college of Medicine & Diversigen Inc, world renowned expert on microbiome and microbiome analysis, diagnostics
Prof. Richard Gallo, MD – UC San Diego, Chair of Dermatology Division of UC San Diego School of Medicine
Prof. Tisa Hatta, MD – UC San Diego, Chief of Dermatology Clinical Trials at UC San Diego
Prof. Raja Sivamani, MD - UC Davis, Clinical dermatologist, acne expert
Tracy Shafizadeh, PhD – Metabolome Inc, metabolite research expert
John Newsam, PhD – Tioga Inc, Formulation expert

Ownership structure
Dermala has raised $250,000 in investments to date. The technology development has been supported by government grants including previous STTR/SBIR and R21, R01 grants from NIH.

Capitalization table (as of November 2015)

	Number of shares	%
Co-founders		70.00
Angel investors		20.00
Board Members		2.00
Employees		8.00
Total	**15,000,000**	**100.00**

Product

Product Description: Human Microbiome-based Therapy for Chronic Diseases

Dermala's approach to preventing and treating chronic diseases (see Figure 1) consist of sequencing the microbiome to characterize and properly diagnose the dysbiosis in the microbiome followed up human microbiome-based therapeutics and maintenance treatments. The therapeutics consists of microbiome-derived compositions that upon application restore the balance in the human microbiome which results in disease elimination. The maintenance treatments preserve the proper balance in the microbiome to prevent disease recurrence. The microbiome-derived therapies are regulated by FDA and have to undergo human clinical testing prior to introduction to market.

Product Pipeline

Dermala is developing multiple products for multiple indications (see Figure 4).

Figure 4. Dermala's Product Pipeline.

Indication	Acne	Yeast infection	Bacterial vaginosis	Urinary tract infection	Atopic dermatitis
Current treatment	Me-too products with limited effectiveness and side effects	OTC and prescription antifungals, problems with disease recurrence	Antibiotics, problems with resistance and disease recurrence	Antibiotics, problems with resistance and disease recurrence	Limited treatments, no cure, recurrence & flareups
Go to market	Prescription, co-formulation with existing therapies is an option	Prescription	Prescription	Prescription	Prescription
FDA approval	Required	Required	Required – Fast-track and GAIN	Required – Fast-track and GAIN	Required – Fast-track and GAIN
Product development risks	Low	Medium	Medium	Medium	Medium-High
Market risks	Medium	Medium	Medium	Medium	Low

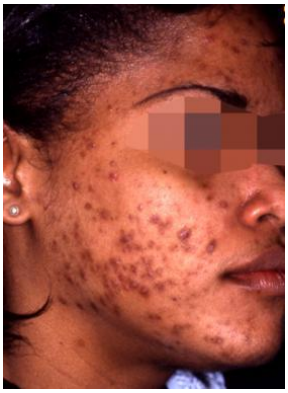
Product Development Strategy

- **Prove the technology on acne vulgaris**
  - Unmet need exists
  - Relatively easy to work with
  - Understood regulatory strategy
  - Subjects available
  - Inexpensive & fast clinical trials
  - Options: Rx & OTC co-formulation

- **Expand to other chronic diseases including**
  - Atopic dermatitis
  - Urinary tract infection
  - Bacterial vaginosis
  - Yeast infection

Product 1: Acne

Problem



- Acne: chronic inflammatory skin disease
- Most prevalent skin condition (up to 95% of individuals), 8th most prevalent disease globally
- All ethnic groups, both genders
- 700M individuals globally (up to 10% of population)
- 40–50 million U.S. individuals have acne, with an 85% prevalence rate in those aged 12–24 years. In 15–20% of individuals acne is moderate to severe.
- Acne is a chronic disease and can persist into adulthood.
- 64% of those aged 20–29 years and 43% of those between 30 and 39 years have visible acne
- 3% of men and 5% of women have acne between the ages of 40 and 49

Unmet clinical needs

- Current treatments do not meet patients' needs.
- Low treatment compliance due to side effects (mainly skin irritation) and limited efficacy (within a short period of time).
- Lack of safe and effective treatments for pregnant females
- Unmet clinical need(s)
  - Reduced/no side effects
  - Improved efficacy, better outcomes for inflammatory acne
  - Faster results, easy treatment regiment
  - Do not cause antibiotic resistance
  - Improved patient compliance
  - Suitable for pregnant females

Market Analysis

- **Market projections**
  - ~$7B market (~$3B OTC & $4B Rx) by 2017
  - CAGR 3.9%
- **Unmet market needs and opportunities**
  - 40% of individuals with acne do nothing (due to side effects, limited results with existing treatments, complicated treatment regiments) => market opportunity
  - No innovation for 30 years => market opportunity
  - Current products are reformulated generics => market opportunity
  - Customers prefer "organics" => market opportunity
  - Comprehensive/integrated Dx + Rx approach => market opportunity
- **Target market segments**

- Rx treatment for inflammatory acne in individuals who cannot tolerate benzoyl peroxide with *P. acnes* strains resistant to antibiotics.
- Treatment for pregnant women.

Solution

Novel topical antimicrobials for the treatment and prevention of acne. The proposed API, DRM1, has been derived from *S. epidermidis*, a **commensal** bacterium present on normal skin. Proposed delivery – topical application.

Competition (existing)

- Treatment options: OTC (over the counter) and Rx (prescription)
  - Reformulated benzoyl peroxide (Neutrogena, Proactive, Clerasil)
  - antibiotics (Solodyn)
  - topical retinoids or
  - oral isotretinoin (Accutane)

- Companies
  - Guthy-Renker, Johnson & Johnson, Reckitt Benckiser, Stiefel (GSK Company), Valeant Pharmaceuticals, Actavis, Allergan

Competitive products (existing)

- Benzoyl peroxide (BPO), the most frequently used topical agent for the treatment of mild acne, is an oxidizing agent that causes skin irritation with symptoms of burning, erythema, peeling, dryness, and contact allergy. In 2014, the Food and Drug Administration issued warning that the use of acne products containing active ingredients BPO or salicylic acid can cause rare but serious and potentially life-threatening allergic reactions or severe irritation.
- Antibiotics clindamycin, erythromycin, azithromycin, doxycycline and minocycline, which are used for acne treatment, pose various side effects that range from colitis, gastrointestinal tract dyspepsia, vaginal candidiasis, photosensitivity, enamel hypoplasia, yellowish discoloration of the forming teeth, vertigo, dizziness, and hypersensitivity syndrome.
  - The most important adverse effect for using antibiotics is the development of bacterial resistance. Clindamycin and erythromycin resistant *P. acnes* strains with 23S and 16S RNA mutations are widely distributed. Additionally, new resistant mechanisms are evolving in *P. acnes* with unidentified mutations. Resistance of *P. acnes* to antibiotics is associated with treatment failures and rise of *P. acnes* as an emerging pathogen. There are increasing reports of infections caused by resistant *P. acnes* in non-acne patients such as post-surgery.
  - 60% of *P. acnes* in individuals with acne are resistant to antibiotics in U.S., up to 90% in Europe
- **Topical retinoids**, derivatives of vitamin A, prevent comedone formation with 40 to 70% reported effectiveness but are accompanied with **skin irritation**, dermatitis and associated erythema and burning sensation, photosensitivity and acne flare-ups.
- **Oral isotretinoin**, which is indicated for severe acne, is a potent teratogen (-> **birth defects**) and women of child bearing age require negative pregnancy test prior to treatment and strict contraceptive measures before, during and even 6 weeks post therapy. Isotretinoin can also result in serious side effects, including suicidal thoughts, headaches, and those of musculoskeletal, ophthalmic, and central nervous systems.

Competition (potential)

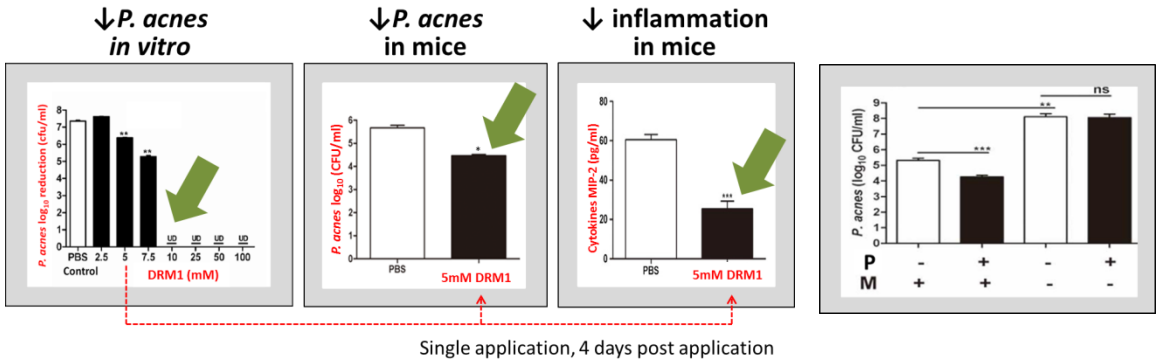
Company	What they do	How Dermala compares
Acne new product development AOBIOME **Angel funded** novantherapeutics **$50M VC funded** DERMIRA **Public company**	**AOBiome**: uses nitric oxide (NO) producing soil bacteria => have to be reapplied, are killed by sunscreen, makeup, skincare. **Novan:** uses topical NO (similar to AOBiome) **Dermira:** targets sebum	**Dermala** focuses on a microbiome-derived small molecules => ↓side effects. Dermala's candidate can be used with any other skincare products and can be co-formulated with existing therapeutic agents => better results.
Microbiome companies µBiome Diversigen **VC funded**	Focus on sequencing microbes, not on drug development	**Dermala** focuses on drug development. We outsource sequencing to these companies.
Microbiome companies VEDANTA BIOSCIENCES SECOND GENOME THE MICROBIOME COMPANY MicroBiome therapeutics **VC funded** SeresHealth 4D pharma plc **IPOs (Seres $140M IPO in June '15, market cap $1.9B in Sept '15, in Ph2 clinical trials)**	Focus on gut – Crohn's, IBD, ulcerative colitis, etc.	**Dermala** focuses on skin diseases. We track gut microbiome companies (including their FDA approaches) and learn from them.

Lead Product Candidate for Acne: DRM1 prototype

Current state of development: DRM1 (see Figure 5)

- Proof of concept demonstrated in mice -> reduction of P. acnes and reduction of inflammation
- Favorable safety & toxicity completed -> superior to current therapies
- No skin irritation & sensitization observed -> superior to current therapies
- Limited effect on skin microbiome -> superior to current therapies
- 3 months stability study completed
- IND enabling studies completed

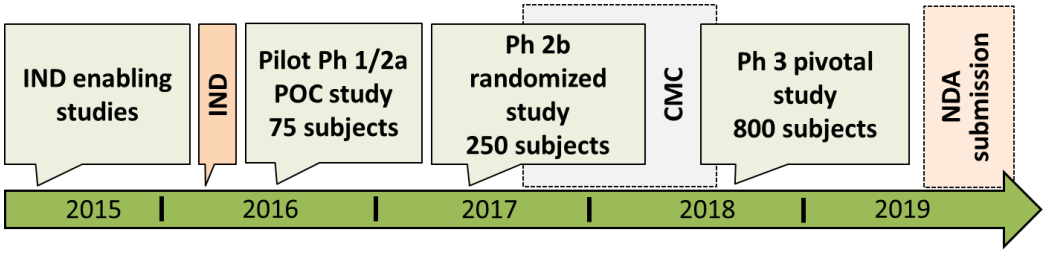
Figure 5. Pre-clinical proof of concept data for DRM1



Clinical Development Plan: DRM1 (see Figure 6)

– Rx treatment for inflammatory acne in individuals who cannot tolerate benzoyl peroxide with *P. acnes* strains resistant to antibiotics.

Figure 6. DRM1: Clinical development plan – human trials



Phase 1/2a Pilot Study: DRM1

- Study Objectives: To assess the safety, tolerability, and efficacy of topical DRM1 in reducing the number of acne vulgaris lesions in patients with acne to that of placebo (vehicle)
- Study design: Single-center, randomized, double-blind, vehicle-controlled, 12-week intervention study
- Sub-Study 1: All subjects – skin microbiome analysis before & after treatment. Sub-Study 2: Five subjects from each group - cytokine profile and number of *P. acnes* bacteria in individual acne lesions before & after treatment.
- Study Population: Generally healthy male and female subjects, ages 12+ years old with clinical diagnosis of acne vulgaris
- Total Number of Subjects: 75
- Treatment Groups: DRM1 dose 1, DRM1 dose 2, placebo
- Duration of Study: 84 days (treatment)/98 days (total)
- Time to Completion: 8 months
- Cost: $500,000
- Study Endpoints
  - Primary Outcome Measures:
    - Change in number of acne lesions on the face at day 84 compared to baseline for subjects in each of the three treatment groups
  - Secondary Outcome Measures:
    - Change in number of acne lesions on subject's bilateral shoulders at day 84 compared to baseline in each of the three treatment groups
    - Change in mean inflammatory lesion counts at days 28, 56, and 84 compared to baseline for subjects in each of the three treatment groups
    - Change in mean non-inflammatory lesion counts at days 28, 56, and 84
    - Change in GAGS and IGA scores at days 28, 56 and 84
    - Determine the effect of DRM1 on the cutaneous microbiome, inflammatory cytokine levels, and P. acnes count in acne lesions at baseline and day 84 for subjects in each of the three treatment groups.
    - Investigators rating of overall improvement and patients self-assessment of overall improvement and cosmetic acceptability
    - Adverse event reports and patient's opinion on local tolerability of the study gels at the end of study

Phase 2b Trial: DRM1

- Study Objectives: To compare safety, tolerability, and efficacy of topical DRM1 in reducing the number of acne vulgaris lesions in patients with acne to that of placebo (vehicle) and current therapy

- Study design: Multi-center, randomized, double-blind, vehicle-controlled, 12-week study
- Study Population: Generally healthy male and female subjects, ages 12+ (requires parental consent) with clinical diagnosis of acne vulgaris
- Total Number of Subjects: 250
- Treatment Groups: DRM1 dose 1, DRM1 dose 2, placebo, antibiotics (or other current therapy)
- Duration of Study: 84 days (treatment)/98 days (total)
- Estimated Time to Completion: 12 months
- Projected Cost: $2M

Phase 3 Trial: DRM1

- Study Objectives: To compare safety, tolerability, and efficacy of topical DRM1 in reducing the number of acne vulgaris lesions in patients with acne to placebo
- Study design: Multi-center, randomized, double-blind, vehicle-controlled, 12-week study
- Study Population: Generally healthy male and female subjects, ages 12+ with clinical diagnosis of acne vulgaris
- Total Number of Subjects: 800
- Treatment Groups: DRM1, Placebo
- Duration of Study: 84 days (treatment)/98 days (total)
- Study Endpoints
  - Primary Outcome Measures: Change in number of acne lesions on the face at day 84 compared to baseline
  - Secondary Outcome Measures: (1) Investigators rating of overall improvement and patients self-assessment of overall improvement and cosmetic acceptability. (2) Adverse event reports and patient's opinion on local tolerability of the study gels at the end of study
- Estimated Time to Completion: 12 months
- Projected Cost: $10M

Product 2: Vaginal Yeast Infection (Candidiasis)

Problem

- Vaginal yeast infection (candidiasis) is one of the most common vaginal infections. It is the second most common cause of vaginal inflammation after bacterial vaginosis.
- Associated with excessive growth of *Candida albicans* (yeast) in the vagina.
- About 75% of women have at least one infection in their lifetime.
- Approximately 20% of women get an infection yearly.
- About 5% of women have more than three infections in a single year.
- About 5-8% of the reproductive age female population will have four or more episodes of symptomatic Candida infection per year; this condition is called recurrent vulvovaginal candidiasis (RVVC).
- Risk factors include taking antibiotics, pregnancy, diabetes, and HIV/AIDS.
- Infection occurs in about 30% of women who are taking a course of antibiotics by mouth.
- During pregnancy, the *Candida* fungus is more common, and recurrent infection is also more likely.
- The most common symptom is vaginal itching, which may be severe.
- Other symptoms include burning with urination, white and thick vaginal discharge, pain with sex, and redness around the vagina.

Unmet clinical needs

- Current treatments do not meet patients' needs.
- Treatment for vaginal yeast infection using antifungal medication is ineffective in up to 20% of cases.
- Recurrence is prevalent
- Lack of safe and effective treatments for pregnant females

Market analysis

- **Market projections and opportunities**
  - The global candidiasis therapeutics market is currently valued at $2 billion
  - CAGR 5.9%
  - The pipeline of innovative new products under development is weak => market opportunity
  - Comprehensive/integrated Dx + Rx approach => market opportunity
  - Prevention of recurrence => market opportunity
  - Prevention of infection during antibiotic therapy => market opportunity
- **Target market segments**
  - Rx treatment and prevention of yeast infection in women with four or more episodes of yeast infection in a year or when severe symptoms of vulvovaginal inflammation are experienced - recurrent vulvovaginal candidiasis (RVVC). Also when coupled with pregnancy, poorly controlled diabetes or poor immune function. About 5-8% of the reproductive age female population will have four or more episodes of symptomatic Candida infection per year; this condition is called recurrent vulvovaginal candidiasis (RVVC).

Solution

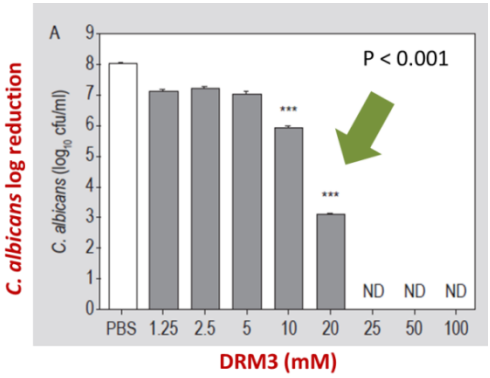
Novel topical antimicrobials for the treatment and prevention of yeast infection caused by *C. albicans*. The proposed API, DRM2, has been derived from *P. acnes*, a **commensal** bacterium present on normal skin. Proposed delivery – moistened wipes, intravaginal inserts.

Competitive analysis (existing)

The following regimens are frequently recommended as treatment:

- Intravaginal agents: butoconazole, clotrimazole, miconazole, nystatin, tioconazole, terconazole
- Oral Agent: fluconazole as a single dose

Lead Product Candidate for Vaginal Yeast Infection: DRM3 Prototype

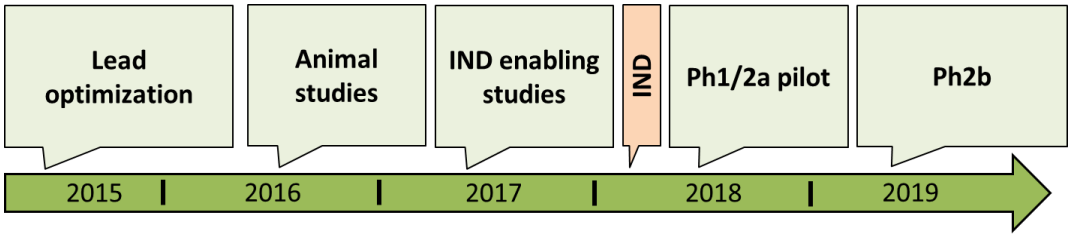


Current state of development: DRM3 (See Figure 7)
In vitro data are available. Results to date demonstrate that DRM3 kills *C. albicans in vitro*.

Figure 7. *In vitro* pre-clinical proof of concept data for DRM3

Product Development Plan: DRM3 (see Figure 8)

Figure 8. Product Development Plan: DRM3



Product 3: Bacterial Vaginosis (BV)

Problem

- BV is the most common vaginal infection in women of reproductive age.
- The percentage of women affected at any given time varies between 5% and 70%.
- In the United States about 30% of women between the ages of 14 and 49 are affected.
- BV is defined by the disequilibrium in the vaginal microbiota with decline in the number of lactobacilli, overgrowth and biofilm formation by *Gardnerella vaginalis*, overgrowth of bacteria.
- BV is a risk factor for pelvic inflammatory disease, HIV, sexually transmitted infections, and reproductive and obstetric disorders. BV in pregnancy may increase the risk of pregnancy complications, most notably premature birth or miscarriage. Pregnant women with BV have a higher risk of chorioamnionitis, miscarriage, preterm birth, premature rupture of membranes, and postpartum endometritis. BV is associated with gynecological and obstetric complications. Data suggest an association between BV, tubal factor infertility, and pelvic inflammatory disease. Women with BV who are treated with vitro fertilization have a lower implantation rate and higher rates of early pregnancy loss.
- Treatment is typically with the antibiotics metronidazole or clindamycin given by mouth or applied inside the vagina.
- About 10% to 15% of women do not improve with the first course of antibiotics and recurrence rates are up to 80%.

Solution

Novel topical antimicrobials for the treatment and prevention of bacterial vaginosis derived from **commensal** bacteria present on normal skin and in normal vagina. Proposed delivery – moistened wipes, intravaginal inserts.

Current state of development

- Candidate selection and testing *in vitro.*

Product 4: Urinary Tract Infection (UTI)

Problem

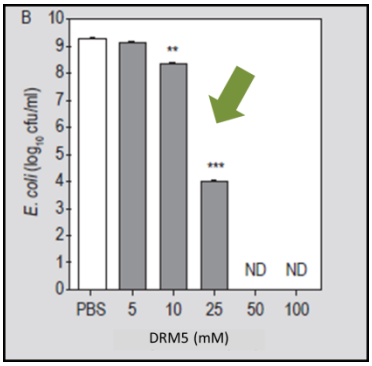
- *E. coli* is the cause of 80–85% of urinary tract infections (UTIs).
- UTIs are the most frequent bacterial infection in women.
- 10% of women get an infection yearly and 60% have an infection at some point in their lives.

- In addition to females, infants, elderly, patients with catheters, patients with diabetes, multiple sclerosis, and AIDS are at risk of UTIs. In elderly, the UTI is the second most common form of infection accounting for nearly 25% of all infections. Catheter-associated UTI is the most common hospital-acquired infection accounting for >1 million cases in hospitals and nursing homes.
- Recurrences are common, with nearly half of people getting a second infection within a year.
- In the U.S., the UTIs account for 7 million office visits, 1 million emergency department visits, and 100,000 hospitalizations every year.
- The cost of these infections is significant both in terms of lost time at work and costs of medical care. In the U.S. the direct cost of treatment is estimated at $1.6B annually.
- The infection is treated with antibiotics but the thread of resistance is a serious problem. For example, fluoroquinolones that are commonly used for the treatment of UTIs are ineffective in more than half of patients in many parts of the world today.

Solution

Novel topical antimicrobials for the treatment and prevention of *E. coli* infection in patients with UTIs. The proposed API, DRM5, has been derived from *P. acnes*, a **commensal** bacterium present on normal skin. Proposed delivery – moistened wipes.

Lead Product Candidate for UTI: DRM5 Prototype



Current state of development (see Figure 9)

- *In vitro* data are available. Results to date demonstrate that DRM5 kills *E. coli in vitro.*

Figure 9. Current state of development: DRM5

Product 5: Atopic Dermatitis (AD)

Problem

- Atopic dermatitis (eczema) is a chronic and relapsing inflammatory skin disease characterized by itchy skin lesions and rashes.
- It is primarily common among infants and children but affect people of all ages.
- AD represents a global public health concern with reported lifetime prevalence ranging between 10%–20% in children and 1%–3% in adults.
- Prevalence is increasing worldwide, with high prevalence in western and developed nations compared with other parts of the world.
- Although atopic dermatitis is not life-threatening, it has a huge impact on economic burden and quality of life of individuals.
- There is no cure for AD.
- Current therapies are not working well.
- Recurrence and flare-ups are major problems.

- The cause of AD is unclear. One possibility is a dysfunctional interplay between the immune system and skin.
- AD is associated with skin microbiome dysbiosis, reduces microbiome diversity and flare-ups are associate with S. aureus overgrowth. Scratching worsens symptoms and affected people have an increased risk of skin infections.

Market analysis

- There are 132M cases of atopic dermatitis in the 9 major markets (US, France, Germany, Italy, Spain, UK, Japan, China, and India). Over 15 million American adults and children have atopic dermatitis. China and India combined contributes 83M cases.
- AD therapeutic sales in the nine major markets are forecast to increase from $3.9 billion in 2012 to $5.6 billion by 2022.
- CAGR is 3.8%

Solution

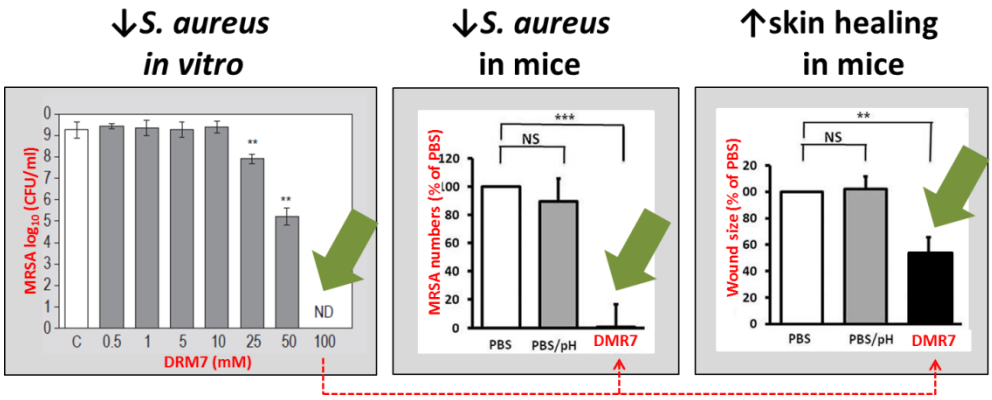
Novel topical antimicrobials for the treatment and prevention of *E. coli* infection in patients with UTIs. The proposed API, DRM7, has been derived from *P. acnes*, a **commensal** bacterium present on normal skin. Proposed delivery – creams.

Lead Product Candidate for Atopic Dermatitis: DRM7 Prototype

Current state of development: DRM7 (see Figure 10)

- Proof of concept demonstrated in mice -> reduction of *S. aureus* and improved healing

Figure 10. Current state of development: DRM7



Business Model and Go-To-Market Strategy

Given the extensive product pipeline, Dermala is using the ”license-out” business model. Under this approach, Dermala will take the initial steps of creating a new product, but then pass the development to a third party (licensor) that will make the products available to the appropriate market. Dermala will be relieved of the burdens of full commercialization. Dermala plans to out-license product verticals to a pharma/consumer product company after a value inflection point, preferably the Ph1/2a pilot trials results which indicate efficacy. The out-licensing will be done in exchange for an upfront fee, milestone

payments, and royalties on net sales. The licensor will finish clinical development and obtain FDA approval. The ideal licensor will have portfolio in specific disease indication, experience in clinical development, manufacturing, sales, marketing and have a potential for obtaining a significant market share.

Dermala will undergo the following activities to successfully out-license its product verticals:

- Strategic planning
- Protecting and strengthening IP
- Value-added development for product candidates in each vertical
- Scouting of potential licensors
- Preparation of pricing scenarios to optimize the mix of upfront and royalty payments
- Identification and analysis of the market
- Determination of the optimal licensing strategy
- Initiation and scheduling of meetings with potential licensors
- Development of the dossier or information package (the basic marketing tool)
- Negotiation of the terms and conditions of the license agreement

There are several potential licensees for Dermala's product candidates, including Valeant, Johnson & Johnson (market leader in acne), Allergan, GSK/Stiefel, etc.

Other options

- Sell product verticals after Ph1/2a clinical trials

One example of successful transaction is Aczone. Aczone (dapsone) gel 5% is approved for sale in both the United States and Canada and is indicated for the treatment of acne vulgaris in patients age 12 and older. Allergan acquired Aczone in 2008 for $150M from QLT USA, Inc. Allergan launches Aczone in the United States in 2008, and in 2012 Aczone® became the most prescribed, branded topical acne treatment by dermatologists that is not a retinoid in the United States. In 2011, Allergan outlicensed Canadian rights to Aczone to Biovail Laboratories International SRL, a subsidiary of Valeant Pharmaceuticals, Inc. in exchange for a CA$500,000 upfront payment followed by subsequent additional payments based on net sales.

- Partner clinical development after Ph1/2a pilot trial
- or Develop to NDA (if no licensing partner identified/terms not acceptable)

Potential exit options for Dermala

Dermala has multiple exit options to deliver returns to shareholders.
These include:

- Acquisition by a pharma/consumer health company or
- IPO

Examples of recent acquisitions of companies in similar fields:

Buyer	Seller	Amount	Year
Allergan	Kythera (derm)	$2.1B	2015
Valeant	PreCision (acne, AD)	$500M	2014
J&J	Covagen (psoriasis)	undisclosed	2014
Amicus	Scioderm (Epidermolysis Bullosa)	$875M	2014

Examples of recent IPOs by companies in similar fields:

Company	IPO amount	Year
Dermira (derm – acne, psoriasis, etc)	$125M	2014
Revance Therapeutics (derm)	$96M	2014
Aclaris (derm - seborrheic keratosis)	$86M	2014
Seres Therapeutics (microbiome – gut)	$140M	2014

Intellectual Property and Barriers to Entry

Barriers to entry

- Utility patent application (licensed from the University of California)
  - Dermala has worldwide exclusive license
- Several provisional patent applications (Dermala)
  - Compound derivatives
  - Formulation and co-formulation
  - Methods of use
  - Multiple disease targets
- Trade secrets
  - Microbiome screening and analysis, formulation screening
- Proprietary microbiome libraries
- FDA exclusivity

Dermala has worldwide exclusive license to IP developed at the UC San Diego. The following patent application has been filed:

Skin probiotic WO 2015106175, PCT/US2015/010926
Priority date: Jan 10, 2014

Abstract:

The disclosure provides skin probiotics, fermented media extract and fermentation byproducts thereof for the treatment of skin disease and disorders as well as for the prevention/treatment of acne and MRSA. In one embodiment, a topical probiotic composition is provided that is capable of producing or maintaining skin microbiome balance. The composition can comprise a therapeutically effective amount or inhibiting effective amount of one or more microbiome balancing compounds.

Claims

- A topical probiotic composition for producing or maintaining skin microbiome balance, the composition comprising therapeutically effective amount or inhibiting effective amount one or more compounds having the structure of …
- The topical probiotic composition further comprising a probiotic commensal skin bacteria fermentation extract.
- Topical probiotic composition comprising a plurality of probiotic commensal skin bacteria.
- The topical probiotic composition wherein the composition is formulated as a lotion, shake lotion, cream, ointment, gel, foam, powder, solid, paste or tincture.
- A method of treating or preventing a skin infection comprising contacting the skin with the topical probiotic composition.
- A method of identifying probiotic commensal skin bacteria, etc.

Funding Needs

Current funding requirements – Projections

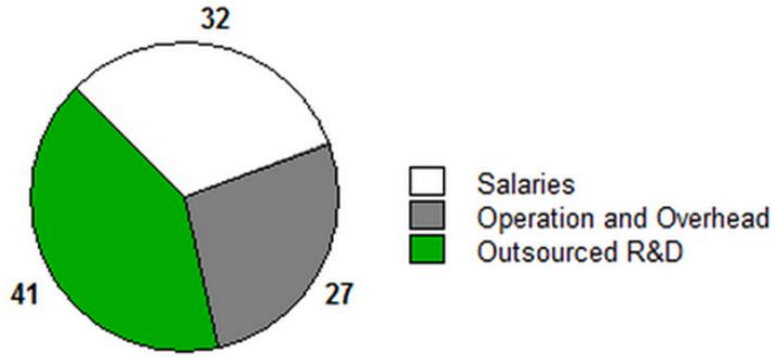
Year	Amount	Use of funds (also see Figure 11)	Source	Form
2015	$250K	Acne: Pre-clinical development, formulation	Angel investor, self	Equity
2016	$900K	Acne: Ph1/2a clinical trials Pipeline development: Pre-clinical studies, selection of lead candidates	Angle investors, venture capital	Equity

Future funding requirements – Projections

Year	Amount	Use of funds	Source	Form
2017	$4M	Acne: Ph2b clinical studies (-> out-licensing) Yeast infection, BV, UTI, AD: IND enabling studies	Venture capital	Equity
2018	$6M	Yeast infection, BV, UTI, AD: IND submission, initiation of Ph1/a clinical studies	Venture capital	Equity
2019	$10M	Yeast infection, BV, UTI, AD: Clinical trials	Venture capital	Equity

Dermala is currently raising funding from angel investors and venture capital.

Figure 11. Use of funds breakdown - 2016.



Financial Projections

Prospective Financial Data

2016 Expense Projections (in thousand dollars)

		Jan	Feb	March	April	May	June	July	August	Sept	Oct	Nov	Dec		Total
Salaries	LR	10	10	10	10	10	10	10	10	10	10	10	10		288
	FB	9	9	9	9	9	9	9	9	9	9	9	9		
	MK	5	5	5	5	5	5	5	5	5	5	5	5		
Operations/overhead		2	2	2	2	2	2	2	2	2	2	2	2		24
Rent		5	5	5	5	5	5	5	5	5	5	5	5		60
Insurance		1	1	1	1	1	1	1	1	1	1	1	1		12
Lab supplies		2	2	2	2	5	5	2	2	2	5	2	2		33
Equipment		0	10	0	0	0	0	0	0	0	0	0	0		10
IP		2	2	2	2	2	2	2	2	2	2	2	2		24
Consultants		2	2	2	2	2	2	2	2	2	2	2	2		24
Outsourced R&D		25	50	50	0	0	0	0	0	0	0	0	0		125
Ph1/2a expenses		20	20	20	20	20	20	20	20	20	20	20	20		240
Other outsourced servi		3	3	3	3	3	3	3	3	3	3	3	3		36
Travel		1	1	1	1	1	1	1	1	1	1	1	1		12
Marketing		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5		6
Monthly burn		87.5	122.5	112.5	62.5	65.5	65.5	62.5	62.5	62.5	65.5	62.5	62.5		894