
*Company Overview*

April 2018

# Peanut Allergy: A Global Problem

- Diagnosis increased 445% in 12 years
- Occurs in 0.5-1.5% of general population of western countries
- Over 3 million peanut allergic in U.S., including 1.5 million children
- Direct costs of childhood food allergies is $6 billion yearly in the U.S. alone
- No approved treatment

Dyer AA et al. *Allergy Asthma Proc.* 2015;36(1):58-64.
Sicherer SH and Sampson HA. JACI 2014;133(2):292-307.
Gupta R et al. *JAMA Pediatr*. 2013;167(11):1026-31.
www.foodallergy.org

# A Novel Solution:
# Oral Mucosal Immunotherapy (OMIT)

Peanut-derived proteins

Specialized toothpaste

Effortless daily administration

**New “Easy-to-Use” Allergy Treatment Platform**

# Benefits of OMIT for Allergy Immunotherapy

**Optimize Efficacy**

- Simple daily administration supports long-term use
- Contacts entire interior of mouth including areas with high concentrations of oral immune cells

**Optimize Safety**

- Limits swallowing and avoids contact with stomach and esophagus
- Controlled time of contact with allergens

**Optimize Usability**

- OMIT replaces your normal toothpaste
- Helps users avoid feeling sick or “not normal”

# Roadmap for Success

## 2018

Crowdfunding campaign

Optimize formulation of Peanut OMIT to FDA standards

Pre-IND and IND meetings with FDA for Peanut OMIT

## 2019

Results of first clinical study of Peanut OMIT (Phase I study)

Initiate development of additional food allergy OMIT products

## 2020 and Beyond

Complete clinical studies of Peanut OMIT (Phase II/III studies)

Obtain FDA and international approvals of Peanut OMIT

# OMIT Advances Peanut Allergy Immunotherapy

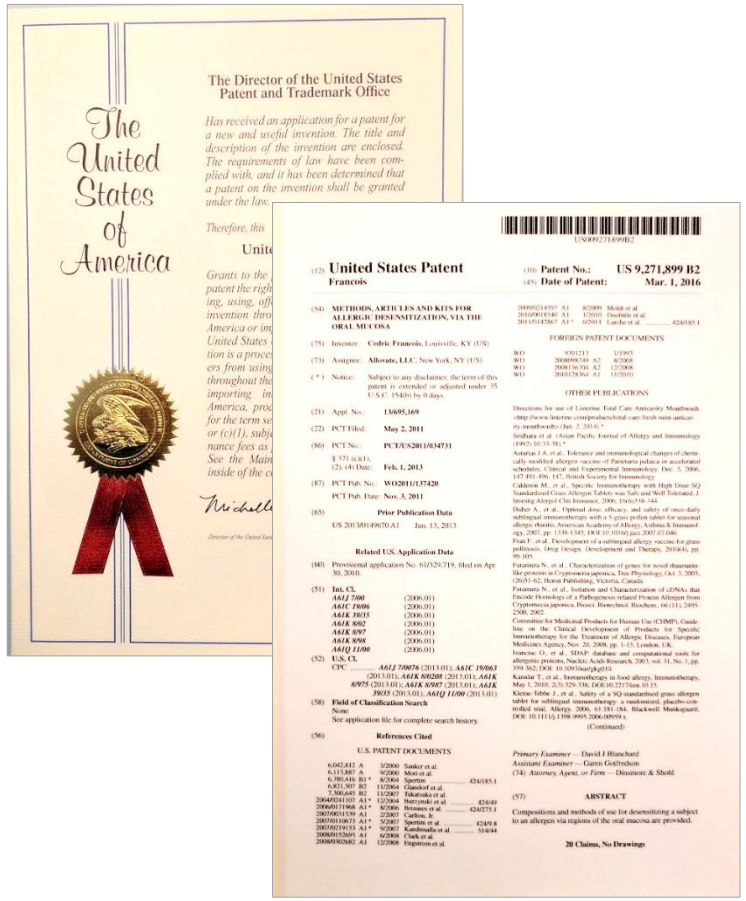
OMIT efficacy demonstrated with non-food allergies*

Studies have shown that therapeutic placement of peanut extracts under the tongue (sublingual immunotherapy or SLIT) can be safe and effective*


*See Scientific Appendix for more info

# OMIT is Protected by Patents

- Platform exclusively licensed for food allergy OMIT
- Initial four OMIT patents issued in United States, Japan, Australia in 2016-2017
- Additional patents pending internationally
- Global protection expected through 2033 and beyond




**Intrommune Has Global Exclusive License For Food Allergy Immunotherapy**

# Competitive Advantages of OMIT

| Daily Immunotherapy Administration | Projected Efficacy | Projected Safety | Support of Long-Term Adherence |
|---|---|---|---|
| Toothpaste (OMIT) | High | Very High | Very High |
| Skin Patch (EPIT) | Low | Very High | Low |
| Ingestion (OIT) | High | Low | Low |
| Placement Under Tongue (SLIT) | Medium | Medium | Low |

# Comparables

| | Intrommune | Aimmune (AIMT) | DBV Technologies (DBVT) |
|---|---|---|---|
| Delivery | Toothpaste **(OMIT)** | Ingestion (OIT) | Skin Patch (EPIT) |
| Ownership | Private | Public | Public |
| Equity Valuation* | $15 million | $1.8 billion | $1.4 billion |

*As of April 11, 2018

# Use of Proceeds

R&D: pre-clinical and clinical development and investigations

CMC: stability testing/manufacturing

Working Capital/G&A

FDA Regulatory: pre-IND interactions and IND filings

Fundraising Fees

# Company Leadership

**Michael Nelson, JD**
Chief Executive Officer
20 years of start-up, finance and legal experience

**Anthony Robinson, MS, CRNP, MBA**
Chief Operating Officer
20 years of clinical and pharmaceutical development experience

**Erick Berglund, PhD**
Chief Scientific Officer
25 years of scientific, start-up, and intellectual property experience

**William Reisacher, MD**
Senior Scientific Advisor & Co-Founder
Associate Professor of Otolaryngology
Weill Cornell Medical College
Associate Attending Otolaryngologist
New York - Presbyterian Hospital

**Wesley Burks, MD, FAAAAI**
Executive Dean UNC Medical School
Distinguished Professor of Pediatrics
Physician in Chief of North Carolina Children's Hospital

**David Fleischer, MD**
Associate Professor of Pediatrics - Allergy
Children's Hospital Colorado
University of Colorado Denver School of Medicine

**Matthew Greenhawt, MD, FAAP, MBA**
Assistant Professor of Pediatrics - Allergy
Children's Hospital Colorado
University of Colorado Denver School of Medicine

**Danya Glabau, PhD**
Founder, Implosion Labs
Faculty, Brooklyn Institute for Social Research
Adjunct Faculty, NYU Tandon School of Engineering

# Thank You

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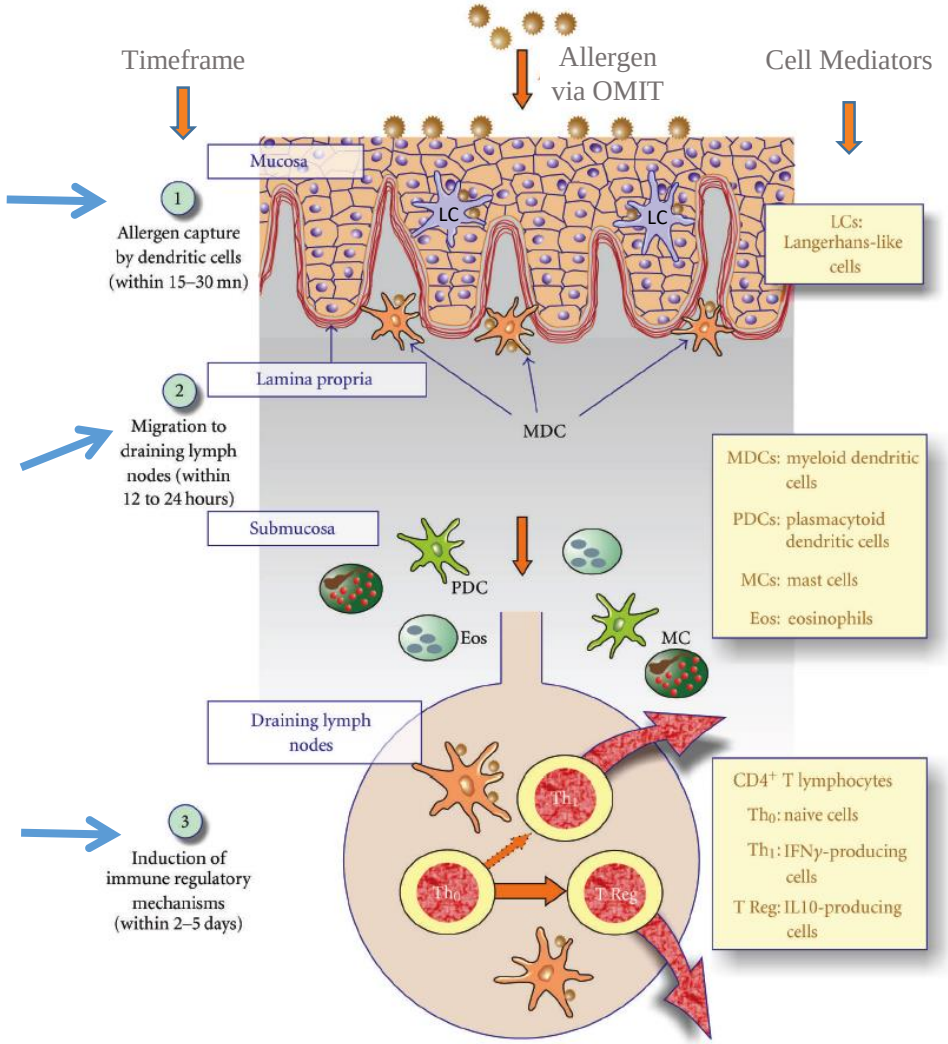
# Scientific Appendix

# Immunology And Biology Of OMIT

1. Following OMIT administration, allergen proteins bind to epithelial cells within minutes, then cross the oral mucosa 15-30 minutes later. Allergen is subsequently captured by Langerhans cells within the mucosa itself and myeloid dendritic cells along the lamina propria. These cells process the allergens into small peptides that are presented in association with MHC class I and class II molecules at the cell surface.

2. Those cells loaded with allergen-derived peptides reach cervical lymph nodes within 12 to 24 hours, where they interact with naive CD4+ T cells to support the differentiation of $Th_1$ and $T_{Reg}$ cells within two to five days.

3. These CD4+ T cells subsequently migrate back to mucosal tissues, resulting in allergen tolerance with down-regulation of preexisting $Th_2$ responses.

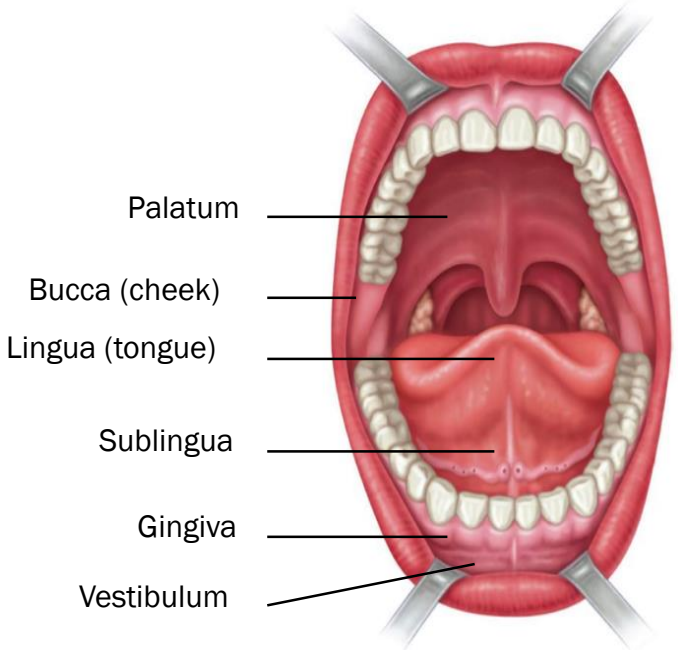


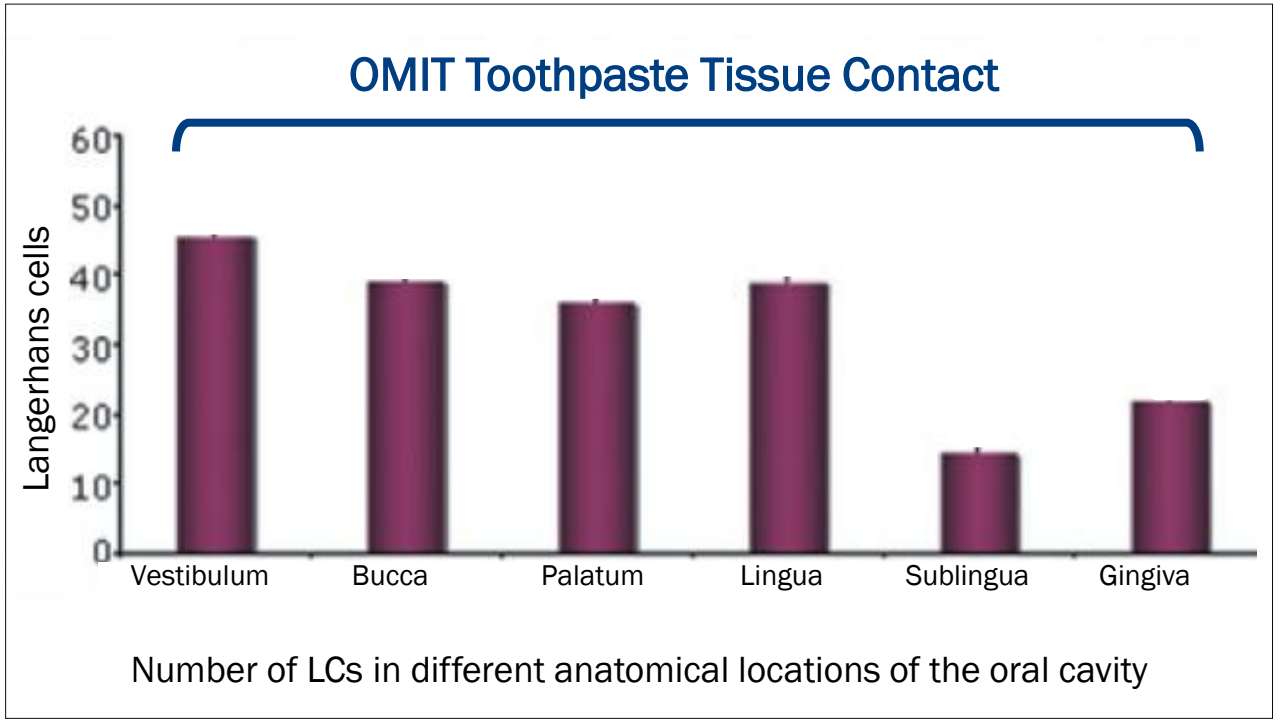


4. $T_{Reg}$ and $Th_0$ cells inhibit $Th_2$ cells, which in turn inhibits $Th_2$ production of cytokines such as IL-3, IL-4, IL-5, and IL-9. These cytokines drive the differentiation, survival and activity of mast cells, basophils, eosinophils – the cells whose disproportionately high populations and errant activation cause the acute clinical symptoms of food allergies, including anaphylaxis.

Adapted from: Moingeon P, and L. Mascarell. Induction of tolerance via the sublingual route: mechanisms and applications. *Clin Dev Immunol.* 2012; Vol. 2012: Article ID 623474.

# OMIT Targets Entire Oral Mucosa




## Optimizes Exposure To Oral Immune Cells

Allam JP, et al. *Allergy*. 2008; 63(6):720-727.

# OMIT Successfully Tested in Non-Food Allergy

| OMIT Respiratory Clinical Investigation | |
|---|---|
| **Location** | Weill Cornell Medical College |
| **Grant Funding** | Empire State Development's Division of Science, Technology and Innovation (NYSTAR) |
| **Size** | 24 allergic rhinitis patients |
| **Duration** | 12 months |
| **Final Patient Enrolled** | June 25, 2014 |
| **Design** | • Open label<br>• 12 patients using OMIT vs. 12 patients using SLIT allergy drops<br>• "Real-World" allergen treatment |
| **Results** | • Safe and efficacious<br>• Supports improved adherence compared to SLIT drops<br>• Reduction in symptom scores and medication use<br>• Biomarker trends (IgE, IgG4) indicate development of immunological tolerance |

Oral mucosal immunotherapy for allergic rhinitis: A pilot study

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ABSTRACT

**Background:** *The sublingual mucosa has been used for many years to apply allergenic extracts for the purpose of specific immunotherapy (IT). Although sublingual IT (SLIT) is both safe and efficacious, the density of antigen-presenting cells is higher in other regions of the oral cavity and vestibule, which make them a potentially desirable target for IT.*

**Objective:** *To present the concept of oral mucosal IT (OMIT) and to provide pilot data for this extended application of SLIT.*

**Methods:** *An open-label, 12-month, prospective study was undertaken as a preliminary step before a full-scale clinical investigation. Twenty-four individuals with allergic rhinitis received IT by applying allergenic extracts daily to either the oral vestibule plus oral cavity mucosa by using a glycerin-based toothpaste or to the sublingual mucosa by using 50% glycerin liquid drops. Adverse events, adherence rates, total combined scores, rhinoconjunctivitis quality-of-life questionnaire scores, changes in skin reactivity, and changes in serum antibody levels were measured for each participant.*

**Results:** *No severe adverse events occurred in either group. The adherence rate was 80% for the OMIT group and 62% for the SLIT group ($p = 0.61$). Decreased total combined scores were demonstrated for both the OMIT group (15.6%) and the SLIT group (22.3%), although this decrease did not reach statistical significance in either group. Both groups achieved a meaningful clinical improvement of at least 0.5 points on rhinoconjunctivitis quality-of-life questionnaire. A statistically significant rise in specific immunoglobulin G4 (IgG4) was seen in both groups over the first 6 months of treatment.*

**Conclusion:** *OMIT and SLIT demonstrated similar safety profiles and adherence rates. Measurements of clinical efficacy improved for both groups, but only changes in IgG4 achieved statistical significance. These pilot data provide enough evidence to proceed with a full-scale investigation to explore the role of OMIT in the long-term management of allergic rhinitis.*

(Allergy Rhinol 7:e21–e28, 2016; doi: 10.2500/ar.2016.7.0150)

Approximately 20–40% of the U.S. population has allergic rhinitis (AR).[1] AR can have a significant impact on the quality of life of the individual and may also lead to further sensitization and the development of asthma.[2,3] Although AR is commonly treated with pharmacotherapy and environmental control strategies, antigen-specific immunotherapy (IT) is currently the only disease-modifying treatment available. Allergenic extracts are delivered either through subcutaneous injection (subcutaneous IT [SCIT]) or by application to the sublingual mucosa (sublingual IT [SLIT]) on a consistent basis for ~3–5 years to achieve a long-term benefit.[4]

Since 1996, SLIT has been recognized as a potential alternative to SCIT by the World Health Organization, and the efficacy of the treatment for both AR and asthma has been confirmed in many randomized controlled trials and meta-analyses.[5–7] However, although the efficacy of both SCIT and SLIT versus placebo has been clearly demonstrated, conclusive head-to-head data are lacking.[8] One systematic review by Dretzke *et al.*[9] failed to demonstrate superiority of one delivery technique over another, whereas a separate systematic review concluded that there was moderate-grade evidence that favored SCIT for the reduction of AR symptoms.[10] In Europe, SLIT represents the majority of new IT prescriptions, and its use has also been increasing in the United States.[11]

Oral Langerhans cells (oLC) are antigen-presenting cells that possess the high affinity receptor for immunoglobulin E (IgE) and the natural protolerogenic characteristics that are necessary for successful IT.[12] Coupled with the production of interleukin 10 and transforming growth factor β, they are able to efficiently bind allergens and present them to T cells in local lymphoid tissue, which leads to an inhibitory effect on T-helper (Th) type 2–mediated (allergic) in-

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*W.R. Reisacher and K. Rochlin are both shareholders for Allovate. W.R. Reisacher is an adviser for Allovate. The remaining authors have no conflicts of interest pertaining to this article*

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Reisacher, W, et al. *Int. J. of Pharm. Compounding.* 2014; 18(4):287-290.

# Peanut SLIT Studies: Precedent for INT-301

| PI/First Author | Study Status | Primary Outcome | Subjects | Duration | Safety | Efficacy |
|---|---|---|---|---|---|---|
| Wesley Burks/Edwin Kim | Published 2011[1] | **1st clinical evidence of desensitization** | **18 children age 1-11** | 12 months, ongoing follow-up | No emergency epinephrine in 4,182 active doses | 20x increase in peanut safely consumed |
| Wesley Burks/David Fleischer | Published 2013[2], 2015[3] | **1st double-blind placebo controlled trial** | **40 subjects age 12-37** | 68 weeks | 1 of 11,854 active doses required epinephrine | Statistically significant desensitization in majority |
| Robert Wood | Published 2015[4] | **Compare efficacy & safety of peanut SLIT (3.7mg/day) vs. OIT (2000mg/day)** | **21 children age 7-13** | 18 months | SLIT significantly superior in safety | SLIT effective; OIT efficacy superior, but 4/11 dropped out |
| Wesley Burks | Ongoing, Interim data[5,6] | **Effect of early intervention** | **50 children age 1-11** | 66 months | No safety issues reported | Desensitization to median 2900mg at 48 months; Sustained unresponsiveness *[interim data]* |
| Robert Wood | Ongoing, unpublished[7] | **Efficacy and safety of dissolving sublingual film** | **15 subjects age 18-50** | 18 months | Unpublished | Unpublished |
| Wesley Burks | Ongoing, unpublished[7] | **FARE-sponsored early intervention** | **50 subjects age 1-4** | 36 months | Unpublished | Unpublished |

[1] Kim E et al. *JACI* 2011(3);127:640-6.
[2] Fleischer DM et al. *JACI* 2013;131(1):119-27.
[3] Burks AW et al. *JACI* 2015;135(5):1240-1248.e3.
[4] Narisety SD et al. *JACI* 2015;135(5):1275-1282.
[5] Hamad A et al. Poster # 193 AAAAI 2017.
[6] Yang L et al. *JACI* 2017 139(2): Abstract 559.
[7] Ongoing, unpublished trials identified through database searches at clinicaltrials.gov