Biotechnology Entrepreneurship Boot Camp

Intrommune Therapeutics

Oral Mucosal Immunotherapy (OMIT):

A Toothpaste Based Approach to Allergy Immunotherapy

June 3, 2019

Safe Harbor

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Oral Mucosal Immunotherapy (OMIT): A New Patient-Adherent Allergy Treatment Platform

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Specific Food-Derived Proteins

Specialized Toothpaste: Keeps Teeth Clean While Stabilizing Allergens

Convenient Daily Immunotherapy Administration

Food-Specific Desensitizing Agents Delivered Via Toothpaste

Peanut Allergy – Peanut INT301 Target Market

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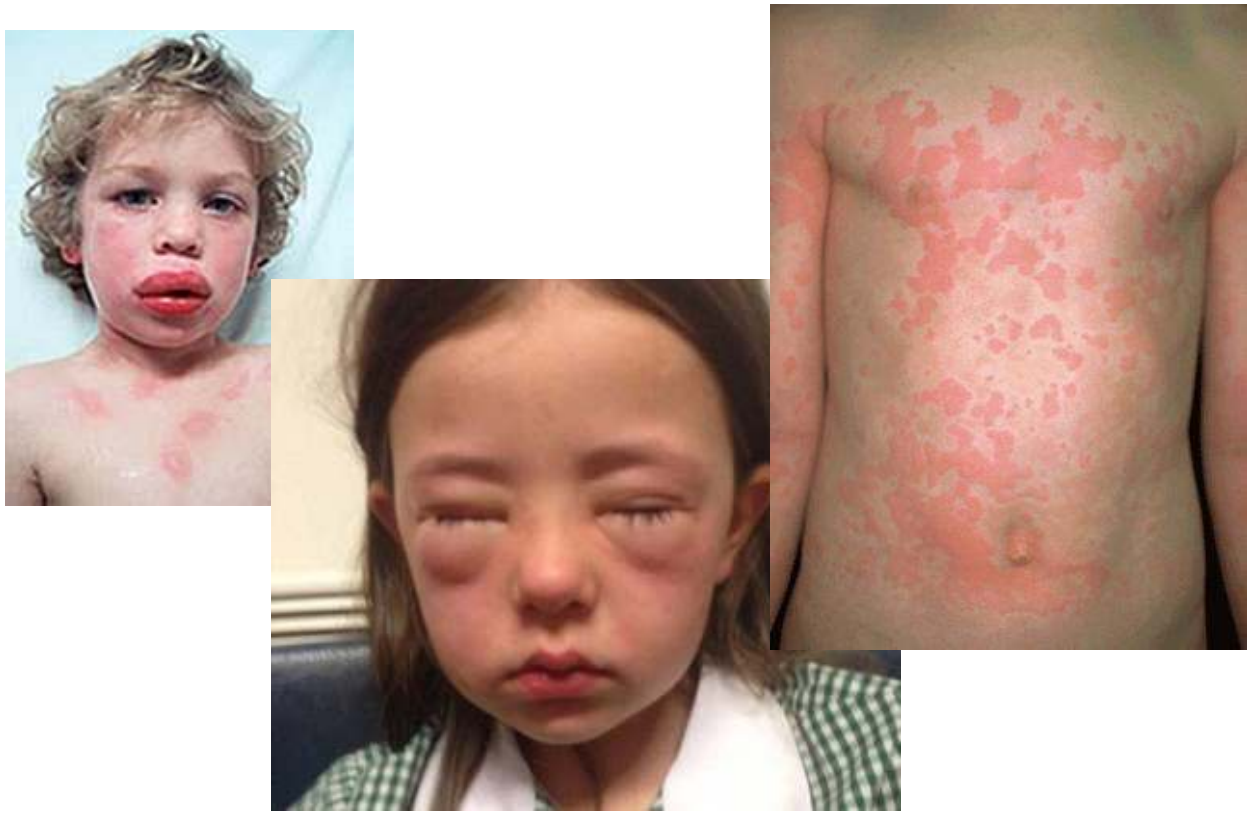


Peanut Allergy

- Over 6mm in U.S. suffer from peanut allergy (~350K in Canada)
  - 1.6mm are children
  - Peanut allergy tripled in children 1997-2008
  - Continues to increase
- Challenges of living with peanut allergy
  - Only option is avoidance
  - High social burden
  - Loss of productivity of caregivers

Patients/Practitioners/Payors Seeking Protection From Accidental Exposure

Serviceable Market Potential for Peanut Allergy

	Peanut Allergy Afflicted Population
US peanut allergic population	6.0 million
US peanut allergic children	1.6 million
77% aged 4-18	1.2 million
83% diagnosed with PA	1.0 million
Assume ~60% will seek medical advice/treatment	600,000
Assume ~2% of adult PA sufferers to seek therapy	90,000
Serviceable Market for Intrommune	**690,000**

Wall Street expectation for PA disease modifying therapy is $5,000-$10,000/patient/year

- Acquisition of 25,000 patients/year (<4% of addressable market) for INT301 to become blockbuster product (>$1 billion annual revenue) at Year 5 at $8,000/patient/year, with patients staying on for average of 5 years

100,000 New PA Sufferers In US/Year

Go-To-Market Strategy (U.S.)

- Presumptive first to market (AIMT) will “condition” market
  - Educate allergists about food allergy therapy
  - Up-dosing procedures training
- Expect CPT codes in place 2021/2022 and wide-scale reimbursement
- Intrommune would need <80 reps to target 5,000 U.S. allergists
  - Initial target will be allergists & select ENTs who offer OIT
  - Present INT301 data at meetings for AAAAI, ACAAI, AAOA, EAACI (Europe), etc.
- Generate stakeholder awareness by partnering with food allergy organizations

FARE Food Allergy Research & Education

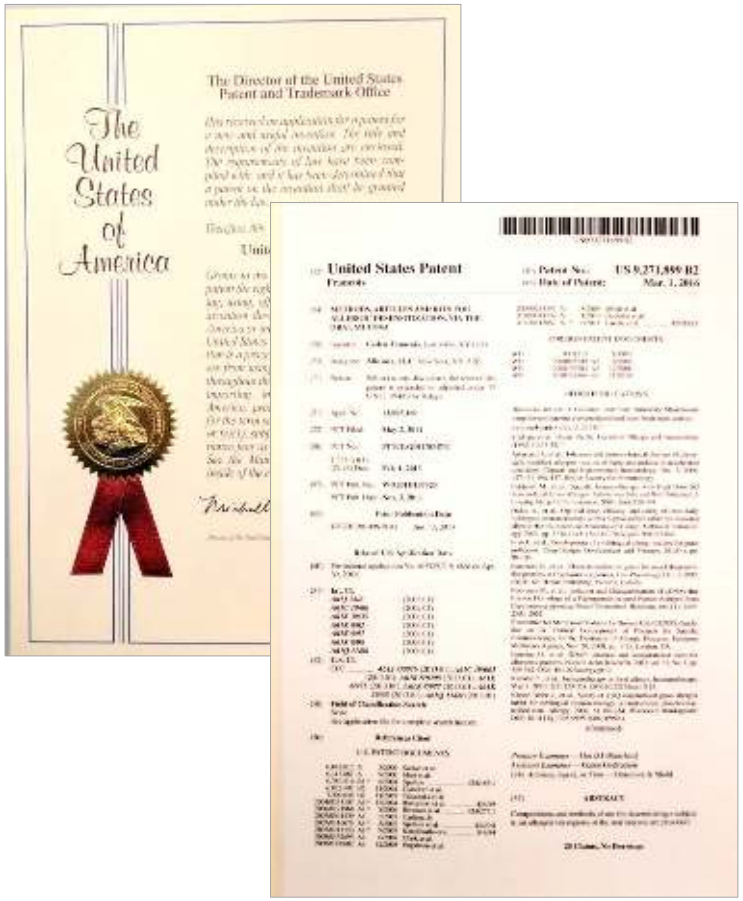
Allergy & Asthma Network

FAACT Food Allergy & Anaphylaxis Connection Team

aafa Asthma and Allergy Foundation of America

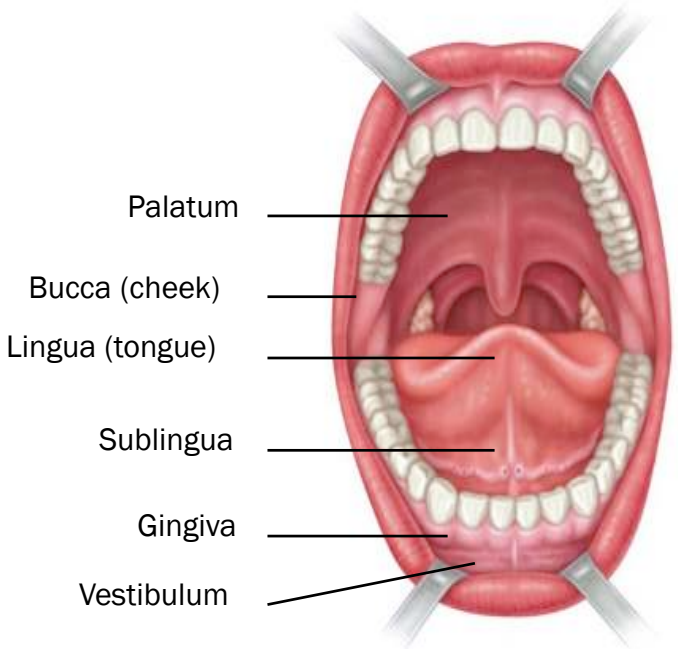
Intellectual Property

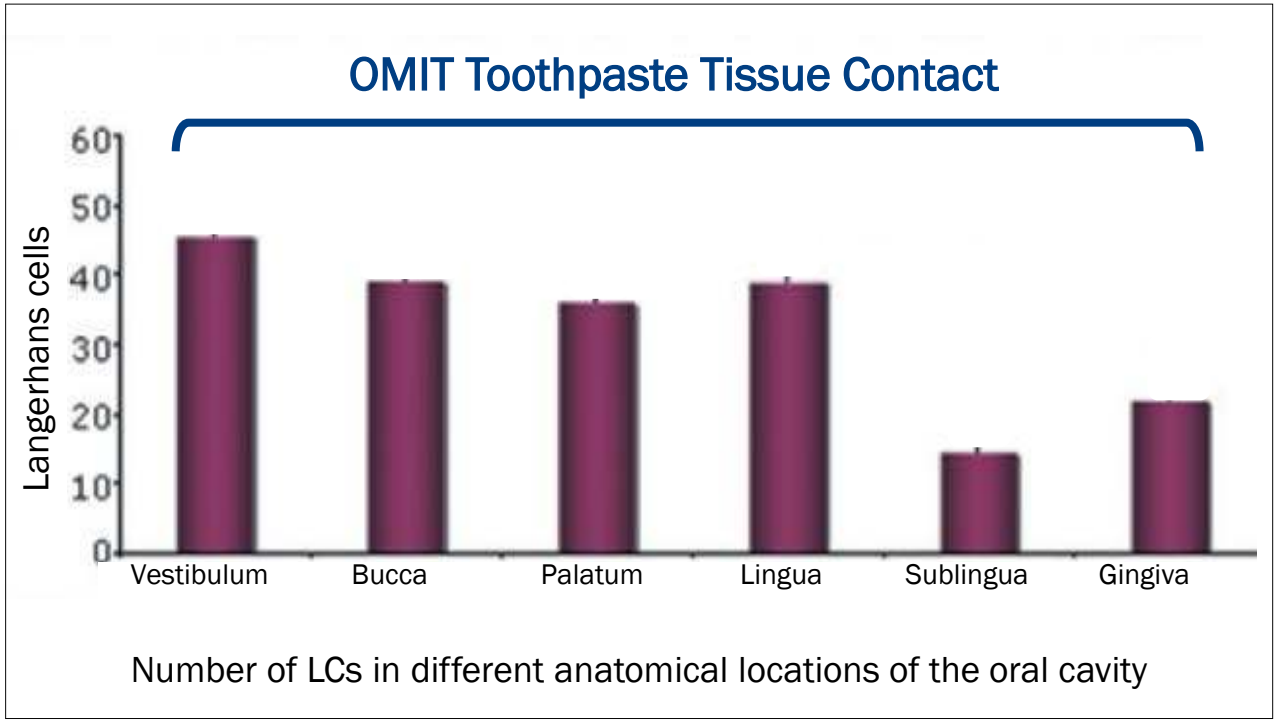
- Global portfolio (includes US, EU, China, India)
- 2 patent families
- 1st patent family covers broad OMIT concept
  - Six patents granted since 2016 (USA, EPO, AUS, JPN)
- 2nd patent family covers formulation
- Global protection expected through 2033
- Additional IP filings planned
- Freedom to operate



Exclusive Global IP License For Food Allergy Immunotherapy

OMIT Targets Entire Oral Mucosa





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

Optimizes Exposure To Oral Immune Cells

OMIT: A Clinically De-Risked Biotech Opportunity

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Sublingual IT for Peanut Allergy is Effective

2016 Clinical PoC OMIT Alleviates Allergic Symptoms

Peanut SLIT Studies: Precedent for INT301

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

OMIT Successfully Tested - Airborne Allergy

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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
Design	• Open label • 12 patients using OMIT vs. 12 patients using SLIT allergy drops • "Real-World" allergen treatment
Results	• Safe and efficacious • Supports improved adherence compared to SLIT drops • Reduction in symptom scores and medication use • Biomarker trends (IgE, IgG4) indicate development of immunological tolerance

Oral mucosal immunotherapy for allergic rhinitis: A pilot study

William R. Reisacher, M.D.,[1] Maria V. Saurma, M.D.,[1] Kate Rochlin, Ph.D.,[2] Maria G. Bremberg, R.N.,[1] and Guy Trupper, M.D.[3]

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 (22.4%), 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 (oLCs) are antigen-presenting cells that possess the high affinity receptor for immunoglobulin E (IgE) and the natural protoallergenic 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-

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

Competitive Advantage: INT301 (Peanut Allergy)

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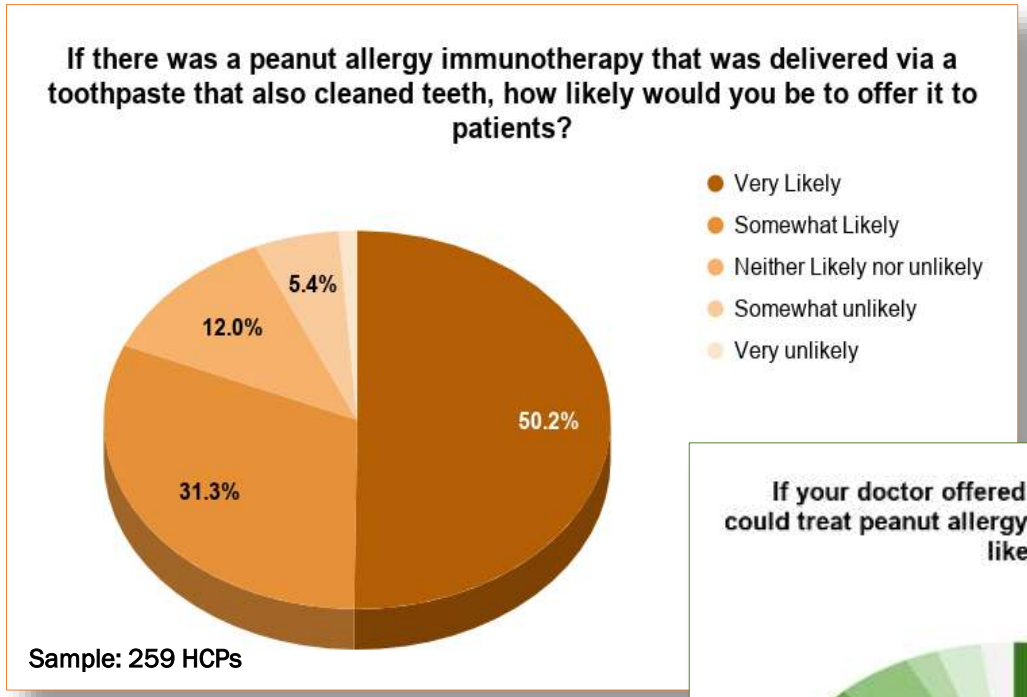
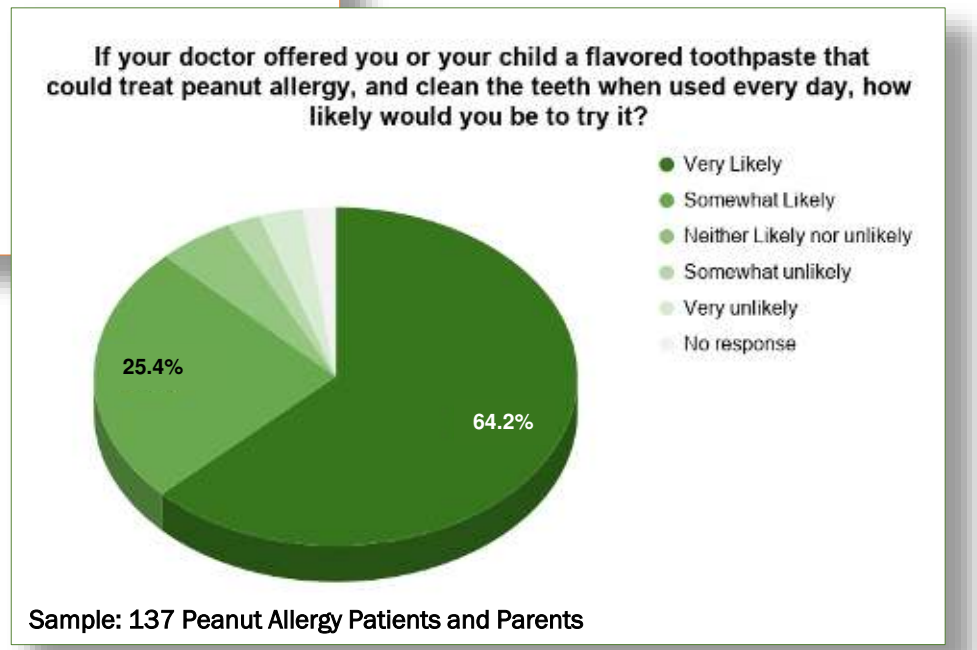
	Efficacy	Safety	Adherence Support	Comment
Oral Mucosal IT (OMIT)	High	Excellent	Excellent	Intrommune Private
Oral IT (OIT)	High	Low	Low	AIMT $1.3B Market Cap 5/13/2019
Epicutaneous IT (EPIT)	Low	Excellent	Low	DBVT $0.6B ($2.4B) Market Cap 5/13/2019 (10/11/2017)

Allergy & Asthma Network Surveys





- ~90% likely to switch patients to new therapy that has fewer side effects
- >80% of doctors and 90% of patients would try OMIT

INT301 Development: Regulatory Strategy

July 2018: Pre-IND meeting with FDA

- Highly collaborative

FDA agrees with Intrommune plans for:

- IND submission
- Phase Ib study in adults with:
  - Abbreviated dosing schedule
  - Safety and tolerance endpoints

Secondary endpoints provide preliminary efficacy information

INT301 Phase 1b Budget Forecast

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Milestone	Milestone Spend	Total Spend	Target Raise
IND Approval	$1.4mm	$1.4mm	$1.4mm
Phase 1: First Dose	$1.6mm	$3.0mm	$8-10mm
Phase 1: Four-Week Draft Safety Read*	$0.6mm	$3.6mm	Strategic Discussions
Phase 1: Results	$1.4mm	$5.0mm	Sale/Partnership /IPO
Phase 2: Go/Start (CMC & Phase 2/3 Trial)**	$3.0mm	$8.0mm	
Approval	$152.0mm	$160.0mm	

Expected Value ~ $50mm

Expected Value $300-$400mm

* DBVT worth $145mm post Phase 1b data

** AIMT worth $650mm post Phase 2a data

Milestones

Intrommune Therapeutics

Completed

- ☑ Obtained Exclusive Rights to OMIT for Food Allergy
- ☑ Designed Clinical Program (AAAAI Ad Board/KOLs)
- ☑ Closed Seed Round
- ☑ Developed INT301 Formulation
- ☑ Pre-IND Meeting – July 2018
- ☑ Angel Led Financing (First Close 2018)

Forthcoming

- ☐ Complete Financing
- ☐ IND Filing – Mid-2019
- ☐ Phase 1B Clinical Trial – 2019
- ☐ Phase 2/3 Launch – 2020

Company Leadership

Michael Nelson, JD
CEO & Co-Founder
New York University School of Law, JD
Cornell University, BS
20 Years of Start-Up, Finance ($2 Billion) Legal Experience

Erick Berglund, PhD
Chief Science Officer & Co-Founder
Goethe University, PhD
Boston University School of Medicine, MS
University of New Hampshire, BS
25 Years of Scientific, Start-Up, and Intellectual Property Experience

Anthony Robinson, MS, CRNP, MBA
Chief Operating Officer
MCP Hahnemann, MS
Pennsylvania State University, MBA
Cornell University, BS
20 Years of Clinical and Pharma Development Experience

Michelle Mantia
Operations Manager
Baruch College, BS
Actuarial Science & 5 Years Project Management Experience

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Key Opinion Leader/Researcher

Tonya Winders
Stakeholder Outreach Advisor
Allergy & Asthma Network CEO
Allergy Mom

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Associate Professor of Otolaryngology
Weill Cornell Medical College
Associate Attending Otolaryngologist
Inventor – Respiratory Allergy Expert

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Cornell University, PhD
Cornell University, MA
Allergy Anthropology Research
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