The Epicutaneous Immunotherapy Company

October 2019
Safe Harbor

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Epicutaneous immunotherapy and Viaskin® Peanut are under clinical investigation and have not been approved for marketing by any health or regulatory authority.
Where We Are Today

Viaskin Peanut BLA accepted for review by U.S. FDA on October 4, 2019
✓ Target action date provided by FDA of August 5, 2020
✓ We believe we remain on track to potentially offer this treatment for peanut-allergic children in 2H 2020

Leadership team expanded and strengthened throughout 2019
✓ Organizational structure in place to support evolution into a potential commercial-stage company
✓ Dr. Pharis Mohideen joined as CMO, bringing extensive clinical drug development experience
✓ Adam Slatter joined as Head of Quality, to help lead BLA remediation process and PAI-readiness preparation
✓ Caroline Daniere joined as CHRO to help build culture and organizational effectiveness, as well as evaluate and refine compensation and reward systems

U.S. launch preparation ongoing with experienced commercial team in place in Summit, NJ
✓ Accomplished pharma commercial leader Kevin Trapp joined as CCO in August 2018

Viaskin Peanut pivotal Phase III data published in JAMA in 1Q 2019
✓ Significant difference in responder rates between Viaskin Peanut and placebo (p<0.001) observed, which we believe suggests that treated patients are less likely to have allergic reactions due to accidental exposures to peanut

3Q 2019 cash position of €73.0 million + approximately €122.8 million in net proceeds from October 2019 financing
Pioneering a New Class of Immunotherapy

• Advancing novel skin immunotherapies for patients with food allergies and other immunological diseases
  – Limited innovation in the field of food allergies has left millions of patients underserved today

• We are focused on discovering, developing and commercializing our novel skin immunotherapy product candidates using our proprietary Viaskin Technology Platform
  – Activation of the immune system with the Viaskin patch
  – No active passage of antigen into the bloodstream
  – Proprietary manufacturing equipment designed, engineered and developed by DBV
# Building a Promising Pipeline of Viaskin Product Candidates

<table>
<thead>
<tr>
<th>PROGRAM</th>
<th>INDICATION</th>
<th>DISCOVERY</th>
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<th>PHASE III</th>
<th>FDA Review</th>
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<tr>
<td>Viaskin Peanut</td>
<td>Peanut Allergy</td>
<td>Ages 4-11 (Breakthrough Therapy and Fast Track Designation*)</td>
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<td>Adolescents &amp; Adults</td>
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<tr>
<td>Viaskin Milk</td>
<td>Cow’s Milk Protein Allergy</td>
<td>Ages 2-17 (Fast Track Designation**)</td>
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<td>Viaskin Egg</td>
<td>Hen’s Egg Allergy</td>
<td>Ages 4-17</td>
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<td>Mechanistic Study</td>
<td>Eosinophilic Esophagitis</td>
<td>Ages 4-17</td>
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<td>5 Programs</td>
<td>Undisclosed</td>
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<tr>
<td>Diagnostics with Nestlé Health Science</td>
<td>Cow’s Milk Protein Allergy</td>
<td>Infants</td>
<td></td>
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</tbody>
</table>

* US FDA Breakthrough Therapy and Fast Track designation in children  
** US FDA Fast Track designation in pediatric patients two and older
EPIT: Unlocking the Immune Properties of the Skin with the Viaskin Patch

EPIT targets the immune system on intact skin

• Condensation chamber formed by Viaskin patch allows natural epidermal water loss to solubilize dry antigens
• Langerhans cells capture solubilized antigen in the epidermis
• Keratinocytes help distinguish pathogens from harmless agents, influencing Langerhans cells to generate an appropriate immune response
• Langerhans cells can process antigens and migrate to regional lymph nodes

Transmission of immunogenic information, with no allergen passage to the bloodstream
Merging Science & Technology for Differentiated Drug Development

**Electrospray**: patented patch manufacturing technology that allows for **precise** antigen deposits without adjuvants

**EPIT Activates the Immune System Through Intact Skin**

**Novel Viaskin Technology Platform**

**Patented electrostatic patch with condensation chamber** allows the antigen to penetrate upper layer of epidermis

Food Allergies: A Major Global Unmet Medical Need

• Every 7 minutes a child goes to the emergency room for an allergic reaction to food\(^2\)

• Each year, approximately 150 deaths are due to allergic reactions; most deaths occur in patients who are aware of their allergy\(^3\)

• Food allergies can cause severe, potentially fatal, allergic reactions, including anaphylaxis

• Eosinophilic esophagitis (EoE), a progressive inflammatory disease, is often caused by ingesting foods, such as peanut, milk and egg\(^4\)

• 50% of peanut-allergic patients experience accidental allergen ingestion over a median span of 5.6 years\(^6\)

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Peanut Allergy: A Daily Burden for Patients and Families Worldwide

Avoidance is difficult: **39%** of peanut allergy patients **experience an accidental exposure within ~1 year** of diagnosis¹

Many factors contribute to severity, making reactions unpredictable²

In children with peanut allergy, **more than half of reactions are severe**³

- Caregivers are constantly trying to both prevent and prepare for exposure
- Prevention involves watching and controlling the child’s environment at all times
- Caregivers are always vigilant and ready to intervene

**73%** of caregivers are most concerned with accidental exposure to peanuts in their kids’ daily life⁴

**67%** of caregivers believe it is more difficult to be a parent of a child with a peanut allergy than without⁴

**60%** of caregivers say their stress level has increased because of their child’s peanut allergy⁴

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Our Solution for a Hard-to-Treat Disease

- Contamination leading to peanut consumption is a serious threat\(^1\)
- Estimated detectable peanut residue ranges from 0.025-45mg of peanut protein\(^2\)
- Desensitization therapies could offer significant reduction of the risks associated with accidental exposures \(^1,3,4,5\)

Yet, even amounts of less than 1 peanut kernel can cause severe reactions

Balancing risk-benefit drug profiles for these patients has been a difficult task for the field

Viaskin Peanut Leads Our Food Allergy Pipeline

• Patients treated with Viaskin Peanut 250 µg were only exposed to ~1 peanut via the skin after 3 years\textsuperscript{1,2}

• Favorable tolerability observed in clinical trials of Viaskin Peanut to date
  - No cases of severe anaphylaxis due to treatment reported
  - Drop-out rate due to AEs < 2% after 12 months (Phase I, Phase II and Phase III trials)
  - Over 95% compliance observed for up to three years of treatment
  - Most commonly reported AEs are mild to moderate application site reactions

• Consistent treatment benefit observed in multiple clinical trials
  - Statistically significant higher rate of responders compared to placebo after 12 months of treatment in Phase II and Phase III trials
  - Increase in CRD to peanut protein versus baseline observed between Viaskin Peanut and placebo after the first year of treatment
  - Exploratory analyses showed that changes in peanut-specific biomarkers support the immunomodulatory effect with Viaskin Peanut
  - Viaskin Peanut 250 µg has demonstrated potential desensitization after 12, 24\textsuperscript{1,2} and 36\textsuperscript{1,2} months of treatment

PEPITES Pivotal Phase III Trial Results (Fleischer, JAMA 2019)

Pivotal Global Randomized DBPC Phase 3 Trial

- 356 children aged 4 to 11 years
- 31 study locations (United States, Canada, Australia, Germany, and Ireland)

Primary Endpoint

Treatment responder definition (assessed using DBPCFC)
- For patients with a M0 ED ≤ 10 mg: responder if ED ≥300 mg at M12
- For patients with a M0 ED > 10 mg and ≤ 300 mg: responder if ED ≥1000 mg at M12

Food Challenge Symptom Scoring

- Food challenges were discontinued when objective signs/symptoms emerged meeting prespecified stopping criteria requiring treatment
- Subjective symptoms (eg, abdominal pain or oropharyngeal itching) were assessed and recorded, but alone were insufficient to stop the challenge

*Subjects were randomized 2:1, stratified by ED, to receive either Viaskin Peanut 250 µg or placebo patch. DBPC= double-blind, placebo-controlled; DBPCFC=DBPC food challenge; ED=eliciting dose; M=month.
Trial Population Included Patients with Multiple Allergic Conditions (Fleischer, JAMA 2019)

- Patient population included a high percentage of subjects with additional allergic conditions

356 Patients Randomized, n (%)
- Active (VP250 μg): 238 (67%)
- Placebo: 118 (33%)

Peanut Eliciting Dose (mg)
- Median: 100
- Mean: 140

Age, years, median (Q1, Q3)
- Active: 7 (6,9)
- Placebo: 7 (5,9)

Gender, n (%)
- Male: 218 (61.2%)
- Female: 138 (38.8%)

Medical History of Patients*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percent of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyallergic</td>
<td>85.7%</td>
</tr>
<tr>
<td>Eczema/Atopic Dermatitis</td>
<td>61.2%</td>
</tr>
<tr>
<td>Allergic Rhinitis</td>
<td>55.9%</td>
</tr>
<tr>
<td>Asthma</td>
<td>47.5%</td>
</tr>
</tbody>
</table>

*Medical History displayed as summary of the trial population. VP250 μg patients: polyallergic n=205 (86.1%), eczema/atopic dermatitis n=139 (58.4%), allergic rhinitis n=132 (55.5%), asthma n=117 (49.2%); placebo patients: polyallergic n=100 (84.7%), eczema/atopic dermatitis n=79 (66.9%), allergic rhinitis n=67 (56.8%), asthma n=52 (44.1%).

Primary Efficacy Outcome Showed Statistically Significant Treatment Effect (Fleischer, JAMA 2019)

- After 12 months, a significantly larger percentage of participants responded to Viaskin Peanut treatment vs placebo patch 35.3% vs 13.6% ($P<0.001$)
- The prespecified 15% lower bound of the 95% CI of the difference between treatment groups was not met (95% CI: 12.4, 29.8)
  - The authors of the publication concluded that the clinical relevance of this is not known

![Response Rate (ITT)]

CI=confidence interval; ITT=intention-to-treat.
A difference in CRD was observed between the active and placebo groups (*P<0.001*)

The median CRD in participants in the Viaskin® Peanut 250 µg group increased from 144 mg at baseline to 444 mg at Month 12

*Nominal P value.

CI=confidence interval; VP=Viaskin Peanut.
Changes in Biomarkers Support Immunomodulatory Effect of Viaskin Peanut (Fleischer, JAMA 2019)

- Levels of IgE increased initially then returned to baseline
- Treatment groups were distinguishable based on levels of peanut-specific IgG4 as early as month 3
  - Levels of IgG4 steadily increased in Viaskin Peanut subjects and were greater than placebo at all time points

PS-IgE Changes Over Time

PS-IgG4 Changes Over Time

IQR=interquartile range; PS=peanut-specific; VP=Viaskin Peanut.
In a post-hoc analysis, 53.1% of subjects on Viaskin Peanut 250 µg increased their baseline ED from ≤100 mg to ≥300 mg, vs only 19% on placebo patch. Based on risk assessment modeling, raising ED from ≤100 mg to ≥300 mg is predicted to reduce the risk of reactions due to accidental exposure by >95%. An increase in ED was 4 times more likely to occur in the Viaskin Peanut group compared to placebo (OR=4.3).

*Based on quantitative risk assessment modeling using national database of consumption data and levels of peanut protein contamination for selected pre-packaged foods.
†Based on ITT population; missing data calculated using mBOCF.

ITT=intention-to-treat; mBOCF=modified baseline carried forward; OR=odds ratio; VP=Viaskin Peanut.
High Adherence and Low Discontinuation Due to TEAEs (Fleischer, JAMA 2019)

- 89.9% of all subjects completed the study, with similar discontinuation rates observed between treatment groups (10.5% in Viaskin® Peanut group, 9.3% in placebo group)
- Treatment adherence* was high (98.5%) across the total population, and comparable between groups
- 4/238 (1.7%) subjects treated with Viaskin Peanut discontinued due to TEAEs
  - 2 due to moderate anaphylaxis; 2 due to skin reactions ≤ grade 3

<table>
<thead>
<tr>
<th></th>
<th>Viaskin Peanut n (%)</th>
<th>Placebo n (%)</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled</td>
<td>238</td>
<td>118</td>
<td>356</td>
</tr>
<tr>
<td>Completed</td>
<td>213 (89.5%)</td>
<td>107 (90.7%)</td>
<td>320 (89.9%)</td>
</tr>
<tr>
<td>Discontinued</td>
<td>25 (10.5%)†</td>
<td>11 (9.3%)</td>
<td>36 (10.1%)</td>
</tr>
<tr>
<td>Due to consent withdrawal</td>
<td>13 (5.5%)‡</td>
<td>6 (5.1%)</td>
<td>19 (5.3%)</td>
</tr>
<tr>
<td>Due to TEAE</td>
<td>4 (1.7%)</td>
<td>0 (0%)</td>
<td>4 (1.1%)</td>
</tr>
</tbody>
</table>

*Defined as the total number of patches applied in the treatment period divided by the number of days in that period.†
‡Additional reasons for discontinuation from the Viaskin Peanut group included lost to follow-up (n=3), noncompliance (n=2), and other (n=3).†
‡Includes one patient who experienced mild anaphylaxis but did not discontinue until 4 days after the event, due to parental consent withdrawal.†

TEAE=treatment-emergent adverse events.
Low Rates of Treatment-Related Serious AEs (Fleischer, JAMA 2019)

- Viaskin Peanut 250 µg: 12 SAEs* in 10 participants (4.2%); Placebo: 6 SAEs in 6 participants (5.1%)
  - 4 SAEs in 3 Viaskin Peanut participants considered related to treatment (1 probably related, 3 possibly related)
  - All were moderate anaphylaxis without evidence of cardiovascular, neurologic, or respiratory compromise
  - All resolved with standard treatment, including 1 dose of epinephrine per participant

*Serious AE defined according to the International Conference on Harmonization-Good Clinical Practice as any untoward medical occurrence that at any dose results in death; is life-threatening; requires hospitalization or prolongation of existing hospitalization; results in persistent or significant disability or incapacity; is a congenital anomaly or birth defect; is an important medical event that may not be immediately life-threatening or result in death or hospitalization but that may jeopardize the participant or require intervention to prevent one of the above outcomes.

AE=adverse event; SAE=serious adverse event.
Expanding to Toddlers: Part B of Phase III Study of VP in Ages 1-3 Initiated in October 2018

Clinical Trial Patient Population

- Children ages 1-3 with peanut allergy
  - > 0.7 kU/L peanut-specific IgE and ≥ 6 mm SPT* wheal
  - Reactive dose at M0 ≤ 300 mg peanut protein

Efficacy Endpoints

Primary endpoint at M12\(^1\)

- Treatment responders (%) in active group compared to placebo at DBPCFC:
  - For patients with a M0 ED** ≤ 10mg: responder if ED ≥ 300 mg at M12
  - For patients with a M0 ED > 10mg: responder if ED ≥ 1,000 mg at M12

Main secondary endpoints: CRD***, changes in peanut sIgE and sIgG4

\(^1\) The primary analysis evaluating the difference between Viaskin Peanut 250 µg and placebo is defined by reaching a lower bound of the two-sided 95% confidence interval (CI) of ≥15%.

\(^2\) An interim analysis will be conducted by the DSMB after the first 50 patients have received 6 months of active treatment to assess the relative change in IgG4 levels in patients treated with Viaskin Peanut 250 µg compared to placebo (n=25).

\(^\#\) Denotes a completed food challenge; Denotes a pending food challenge
Viaskin Milk: Milk Allergy (CMPA) Phase II Study
Identified Safe/Effective Dose for Children

**Clinical Trial Patient Population**

- Children (2-11) and adolescents (12-17)
- Highly sensitive to milk (≥ 10 kU/L milk-specific IgE and ≥ 6 mm SPT* wheal)
- Reactive dose at baseline (M0) ≤300 mg cow’s milk protein (CMP) (~ ≤ 9.4 mL of cow’s milk)

**Efficacy Endpoints**

**Treatment responder definition at M12:**

- ≥ 10-fold increase in CRD** and at least 144 mg of CMP
- OR CRD ≥ 1,444 mg

**Key secondary endpoints:**

- Change from baseline in IgE, IgG4

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**Footnotes:**

* SPT: Skin Prick Test
** CRD: Cumulative Reactive Dose at Food Challenge
*** Protocol change implemented in August 2018 to switch all patients to 300 µg (from 500 µg) for treatment up to 24 months

Denotes a completed food challenge; Denotes a pending, optional food challenge
MILES Results: Support Viaskin Milk 300µg as the Potential First Treatment for CMPA in Children 2-11

**Favorable safety, tolerability and compliance**

- Overall discontinuation rate of 4.5%
  - 1.5% dropout due to AEs
- Most AEs related to application site (mild to moderate)
- No severe anaphylaxis
- No SAEs or epinephrine related to treatment
- Treatment adherence was high
  - Mean patient compliance > 95%

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**Response Rate (ITT*)**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% of Responders (90% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>32.5% (n = 40)</td>
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</tr>
<tr>
<td>150 µg</td>
<td>34.2% (n = 38)</td>
<td>p = 0.042</td>
</tr>
<tr>
<td>300 µg</td>
<td>57.9% (n = 38)</td>
<td>p &gt; 0.999</td>
</tr>
<tr>
<td>500 µg</td>
<td>38.9% (n = 36)</td>
<td>p = 0.733</td>
</tr>
</tbody>
</table>

* Missing data: failure imputation (considered as non-responders) in ITT population

P-values obtained using exact logistic regression

ITT, Intent-to-Treat
DBV Technologies: Pioneering a New Class of Immunotherapy

- Leadership team expanded and strengthened in 2019
- BLA for Viaskin Peanut in children ages 4-11 accepted for review in October 2019, with target action date of August 5, 2020
- Phase III clinical program for Viaskin Peanut in children ages 4-11 completed (PEPITES & REALISE trials) in 2018
- Positive preliminary Phase I/II data in second food allergy candidate, Viaskin Milk
- Key commercial roles, including Kevin Trapp, Chief Commercial Officer, recruited and onboarded in Summit, New Jersey office
- Continuing to build a talented team with offices in US and France
- 3Q 2019 cash position of €73.0 million + approximately €122.8 million in net proceeds from October 2019 financing
APPENDIX
Viaskin Platform
The Skin Has Important Immune Properties

• Immune functions of the skin include
  – Responding to trauma, toxins, and infectious agents
  – Maintaining self-tolerance, preventing allergy, and inhibiting autoimmunity

• Keratinocytes
  – Distinguish pathogens from harmless agents
  – Influence nearby Langerhans cells to generate an appropriate immune response

• Langerhans cells
  – Antigen-presenting cells that can process antigens and migrate to regional lymph nodes

Proprietary & Patented Manufacturing Capabilities Developed by DBV

• Modular components → technology versatility
  – Highly scalable
  – Broadly applicable platform

• Manufacturing capabilities
  – In-house development and engineering of electrospray machines
  – Development and engineering expertise at DBV
Core Innovation: Differentiated Electrospray Technology

- **Dose flexibility**
  - Biological API deposit between 20 and 500 µg/cm²
- **API stability**
  - Solid & soluble protein layer, no glue
- **Homogeneous repartition of API**
  - Uniform delivery into skin
- **Replicability**
  - High dosage control in each patch
- **Bioavailability**
  - High solubility from electrostatic forces instead of glue
Robust IP Portfolio: Core Technology, Broad MoAs & Specific Indications

- **Epicutaneous Vaccination**
  - Boost Vaccination
  - Epicutaneous Desensitization

- **EPIT Food allergies**
  - Milk
  - Peanut

- **EPIT Allergy related diseases**
  - Allergic March
  - Eosinophilic Esophagitis
  - Eczema
  - Hemophilia A
  - Immuno Rebalancing

**Core Technology**
- Viaskin I
- Viaskin II
- Electrospray

**Broad geographic applications**
- USA, Europe, Australia, Canada

**Long patent protection**
- Initial core patents through 2022
- Other key patents through 2029-35

**Innovation-driven patent lifecycle management**
Viaskin Peanut Phase III Program: PEPITES & REALISE
Measuring Efficacy: Double-Blind Placebo-Controlled Food Challenge

- **Standardized GMP challenge matrix**
- **Standardized** semi-logarithmic increase of peanut protein doses (DBPCFC\(^2\) as per PRACTALL\(^3\))
- **Allergic symptoms are graded** from a standardized published protocol\(^4\)
- **Challenge stopped by clear objective symptoms**

<table>
<thead>
<tr>
<th>CATEGORIES</th>
<th>OBJECTIVE SYMPTOMS</th>
<th>GRADE</th>
<th>SUBJECTIVE SYMPTOMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. SKIN</td>
<td>A. Erythematous rash: % area involved</td>
<td>0 1 2 3</td>
<td></td>
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<tr>
<td></td>
<td>B. Pruritus</td>
<td>0 1 2 3</td>
<td></td>
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<tr>
<td></td>
<td>C. Urticaria/Angioedema</td>
<td>0 1 2 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>D. Rash</td>
<td>0 1 2 3</td>
<td></td>
</tr>
<tr>
<td>II. UPPER RESPIRATORY</td>
<td>A. Sneezing/Itching</td>
<td>0 1 2 3</td>
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<tr>
<td></td>
<td>B. Nasal congestion</td>
<td>0 1 2 3</td>
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<tr>
<td></td>
<td>C. Rhinorrhea</td>
<td>0 1 2 3</td>
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<tr>
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<td>D. Laryngeal</td>
<td>0 1 2 3</td>
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<td>III LOWER RESPIRATORY</td>
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<td>IV. GASTROINTESTINAL</td>
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<td>A. Subjective Complaints</td>
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<td></td>
<td></td>
<td></td>
<td>Itchy mouth</td>
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<td></td>
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<td>Nausea</td>
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<td>B. Objective Complaints</td>
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<td>Diarrhea</td>
<td>0 1 2 3</td>
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<tr>
<td>Vomiting</td>
<td>0 1 2 3</td>
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<td></td>
</tr>
<tr>
<td>V. CARDIOVASCULAR</td>
<td>Normal heart rate to bradycardia</td>
<td>0 1 2 3</td>
<td></td>
</tr>
</tbody>
</table>

* DBPCFC in PEPITeS and VIPeS at month 12, in OLFUS-VIPeS DBPCFC included an additional 1,600mg step after the 1,000mg step at month 24 & 36

1. Cochrane et al, Allergy 2012
2. Double-Blind, Placebo-Controlled Food Challenge
3. Sampson et al, JACI 2012
PEPITES Post-Hoc Analysis Using VIPES Responder Definition Suggests Consistent Treatment Effect Observed from Phase II to Phase III
Positive Phase III REALISE Results Support Regulatory Filings for Viaskin Peanut

Positive 6-month safety results confirmed the safety and tolerability profile observed in PEPITES, VIPES and CoFAR6

Clinical Trial Patient Population

Patients 4 to 11 with history of IgE-mediated reactions to peanut
• Including patients with severe anaphylaxis ≥ 14 kU/L peanut-specific IgE and ≥ 8 mm SPT* wheal

Safety & Exploratory Endpoints

Primary endpoint to assess safety at M6
• Treatment Emergent Adverse Events
No oral food challenges are required at baseline
Exploratory endpoints
• Quality of Life Questionnaires (FAQLQ & FAIM)
• Evolution of peanut-specific serological markers over time (IgE, IgG4, SPT wheal)

*SPT: Skin Prick Test
Viaskin Peanut Phase II Program: VIPES, OLFUS-VIPES & COFAR6
**VIPES: Dose-Finding Phase IIb Efficacy and Safety Trial (Sampson, JAMA 2017)**

**Clinical Trial Patient Population**

Highly allergic patients
- > 0.7 kU/L peanut-specific IgE and ≥ 8 mm SPT* wheal
- Reactive dose at M0 ≤ 300 mg peanut protein (ie. approx 1 peanut)

**VIPES & OLFUS-VIPES Efficacy**

Primary endpoint at M12, M24 and M36
- ≥ 1000 mg reactive dose OR
- ≥ 10-fold of the initial reactive dose

Main secondary endpoints:
- CRD**, changes in peanut sIgE and sIgG4

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*Denotes a completed food challenge

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*SPT: Skin Prick Test

**CRD: Cumulative Reactive Dose at Food Challenge
VIPES: Patient Population Snapshot at Baseline

221 patients randomized
- 113 Children (6-11)
- 73 Adolescents (12-17) & 35 Adults (18+)

Highly allergic patients (median)
- Children = 30 mg
- Adolescents & Adults = 100 mg

Very high IgE levels: > 100 kU/L
- 47% of Children
- 38% of All Patients

Medical History of Patients
- Asthma
  - n = 130 (58.8%)
- Eczema/Atopic Dermatitis
  - n = 114 (51.6%)
- Allergic Rhinitis
  - n = 96 (43.4%)
- Polyallergic
  - n = 183 (82.8%)
VIPES: Phase IIb Results Key Conclusions

- Primary endpoint met with Viaskin Peanut 250 µg
  - Greatest response in children ages 6-11 (53.6% vs. 19.4%, p = 0.008)

- Increase in threshold reactivity of peanut protein showed a clear dose response with greatest benefit in the 250 µg arm
  - In the children subgroup, mean CRD* at month 12 was 1211.9 mg (median 444 mg) in active vs. 239.1 mg (median 144 mg) in placebo (p < 0.001)

- Immunological data supports treatment effect

- Favorable safety and tolerability profile
  - 6.3% discontinuation rate (0.9% related to treatment)
  - Most frequent related AEs: local cutaneous reaction > 90% of patients mainly mild and moderate (50% with a duration < 2 months)
  - Median treatment compliance of 97.6%

*CRD: Cumulative Reactive Dose at Food Challenge
VIPES: Primary Endpoint Met Focus On Children (Ages 6-11)

Response rate in children across doses after 12 months

<table>
<thead>
<tr>
<th>Dose</th>
<th>% of Responders (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>19.4%</td>
</tr>
<tr>
<td>50 µg</td>
<td>57.1%</td>
</tr>
<tr>
<td>100 µg</td>
<td>46.2%</td>
</tr>
<tr>
<td>250 µg</td>
<td>53.6%</td>
</tr>
</tbody>
</table>

*p = 0.008*

Increase in CRD in children after 12 months (Mean and Median)*

- Placebo: n = 31, Mean CRD Increase = 60.8 mg, Median = 0.0
- 50 µg: n = 28, Mean CRD Increase = 471.2 mg, Median = 135.0
- 100 µg: n = 26, Mean CRD Increase = 570.0 mg, Median = 114.5
- 250 µg: n = 28, Mean CRD Increase = 1,121.0 mg, Median = 400.0

*p < 0.001

* Excluding missing data
VIPES: Immunological Changes In Children (Ages 6-11) Supports Treatment Effect
**VIPES: Primary Efficacy Endpoint Met Identified Viaskin 250 µg As Phase III Dose**

Response rate across doses after 12 months

- **Placebo**
  - n = 56
  - 25.0%

- **50 µg**
  - n = 53
  - 45.3%

- **100 µg**
  - n = 56
  - 41.1%

- **250 µg**
  - n = 56
  - 50.0%

$p = 0.01$
VIPES: Adolescents & Adults High Placebo Response Rate Distorts Analysis

Patients aged 12-55 response rate across doses

<table>
<thead>
<tr>
<th>Dose</th>
<th>% Responders (95% CI)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>32.0%</td>
<td>25</td>
</tr>
<tr>
<td>50 µg</td>
<td>32.0%</td>
<td>25</td>
</tr>
<tr>
<td>100 µg</td>
<td>36.7%</td>
<td>30</td>
</tr>
<tr>
<td>250 µg</td>
<td>46.4%</td>
<td>28</td>
</tr>
</tbody>
</table>

p = 0.40
**VIPES: Adolescents & Adults Changes From Baseline**

**CRD Indicate Dose Response Trend**

Patients aged 12-55 increase in baseline CRD at 12 months across doses

<table>
<thead>
<tr>
<th>Dose</th>
<th>Placebo</th>
<th>50 μg</th>
<th>100 μg</th>
<th>250 μg</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>25</td>
<td>28</td>
<td>30</td>
<td>28</td>
</tr>
</tbody>
</table>

- **Placebo**: Median = 10.0 mg
- **50 μg**: Median = 0.0 mg
- **100 μg**: Median = 30.0 mg
- **250 μg**: Median = 335.0 mg

Mean CRD Increase (95% CI)

- **Placebo**: Mean = 528.4 mg (95% CI)
- **50 μg**: Mean = 619.2 mg (95% CI)
- **100 μg**: Mean = 842.3 mg (95% CI)
- **250 μg**: Mean = 837.4 mg (95% CI)
VIPES: Adolescents & Adults Immunological Changes
Support Dose Response Trend

Peanut-specific IgE (kU/L)

Peanut-specific IgG4 (mg/L)

Viaskin Peanut 250 µg, n=28
Viaskin Peanut 100 µg, n=30
Viaskin Peanut 50 µg, n=25
Placebo, n=25
VIPES: Post Hoc Analysis Using PEPITES Responder Definition

VIPES Children (6-11 years) - Viaskin 250 µg at M12

**Reported Response Rate**

- Placebo: 19.4% (n = 31)
- 250 µg: 53.6% (n = 28)

**VIPES Response Rate Using the PEPITES Response Criteria**

- Placebo: 6.5% (n = 31)
- 250 µg: 46.4% (n = 28)

p = 0.008

p = 0.0007
**OLFUS-VIPES**: Open-label Follow-up Trial To VIPES Extension Trial To Support Use Of Viaskin Peanut

221 stratified patients, 22 centers in US, Canada, France, Poland, and Netherlands

- **VIPES Dose-finding**
  - Placebo
  - 50 µg
  - 100 µg
  - 250 µg

- **OLFUS-VIPES**
  - M0
  - M12
  - 250 µg
  - M24
  - M26

171 patients opted to enroll in OLFUS (overall 83% roll-over rate from VIPES)
- 97 children and 74 adolescents & adults

**Assessed long-term safety and efficacy**

**Double-Blind Placebo-Controlled Food Challenge (DBPCFC)** administered at month-12 and month-24

**Month-26 DBPCFC to explore “sustained unresponsiveness”**
- Patients unresponsive to CRD* > 1,440 mg at month-24 DBPCFC were eligible to continue study
- Two-month period without treatment or consumption of peanut to assess durability of response

---

*CRD: Cumulative Reactive Dose at Food Challenge

Denotes a completed food challenge
OLFUS-VIPES: Long-term Extension Data Shows Benefit Increases Over Time in Phase IIb Study

Response Rate at OLFUS: Baseline, Year-1 and Year-2

- OLFUS baseline: 57.1% (12/21)
- OLFUS year 1: 80.0% (16/20)
- OLFUS year 2: 83.3% (15/18)

**Excluding missing data**

Cumulative Reactive Dose in OLFUS

- Mean ± 95% CI Observed values, ITT

<table>
<thead>
<tr>
<th></th>
<th>n = 21</th>
<th>OLFUS baseline</th>
<th>OLFUS baseline</th>
<th>OLFUS year 1</th>
<th>OLFUS year 1</th>
<th>OLFUS year 2</th>
<th>OLFUS year 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (mg)</td>
<td>1,440</td>
<td>84.5 mg</td>
<td>1,067.8 mg</td>
<td>1,883.5 mg</td>
<td>2,453.9 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (mg)</td>
<td>1,067.8</td>
<td>1,067.8 mg</td>
<td>1,883.5 mg</td>
<td>2,453.9 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td></td>
<td>(84.5 mg, 1,256 mg)</td>
<td>(1,067.8 mg, 1,883.5 mg)</td>
<td>(1,883.5 mg, 2,453.9 mg)</td>
<td>(2,453.9 mg, 3,025.8 mg)</td>
<td>(2,453.9 mg, 3,025.8 mg)</td>
<td>(2,453.9 mg, 3,025.8 mg)</td>
</tr>
</tbody>
</table>

Results shown for Viaskin Peanut 250 µg

* 1 child discontinued (not related to Viaskin Peanut)
** 2 children discontinued (none related to Viaskin Peanut)

Median relative change = 100 \times (\text{Month } xx - \text{Baseline})/\text{Baseline}

Viaskin Peanut 250 µg, n = 18
OLFUS-VIPES: Long-term Follow-up Data Key Conclusions

Late Breaking Oral Presentation at AAAAI 2017

• In children treated for three years with a 250 µg dose there was a trend of progressive response to treatment as measured by increased response rate, higher CRD* and serological changes
  – Treatment benefit was observed to be long-lasting for three years
  – 83.3% response rate after three years, an increase from 57.1% at OLFUS baseline
  – Mean CRD reached 2,453.9 mg at the end of OLFUS, from 1,067.8 mg at OLFUS baseline

• No decreased compliance or increased frequency of AEs in VIPES patients treated for 24 additional months
  – 95.5 % overall compliance rate was observed throughout the study
  – No SAEs or epinephrine use due to treatment was reported in 36 months
  – Most adverse events were related to application site and were mild to moderate, with decreasing severity and frequency over time

Shreffler et al. AAAAI 2017, #L7
*CRD: Cumulative Reactive Dose at Food Challenge
CoFAR6: Efficacy And Safety – NIAID Sponsored Phase II

221 stratified patients, 22 centers in US, Canada, France, Poland, and Netherlands

Enrollment
n = 75

Entry OFC positive to cumulative dose of < 1044 mg peanut protein

Randomization
1:1:1

250 mg Viaskin Peanut
100 mg Viaskin Peanut
Placebo

Week 52
5044 mg OFC

Week 130
5044 mg OFC
[End of study]

Defined Endpoints

Primary endpoint: Proportion with a treatment success following 52 weeks of blinded treatment

• Passing a 5044 mg OFC* to peanut protein at week 52 OR ≥ 10-fold increase in the successfully consumed dose (SCD) of peanut protein at week 52 compared to baseline OFC

Secondary endpoints:

• Comparison of Viaskin Peanut 100 µg vs Viaskin Peanut 250 µg doses at week 52
• Desensitization and sustained unresponsiveness at week 130
• Incidence of all adverse events
• Changes in immune markers


*OFC: Oral Food Challenge

Denotes a completed food challenge. Denotes a pending food challenge
CoFAR6: Primary Endpoint Was Met

- No SAEs or Epinephrine due to drug
- 96% compliance
- Primary endpoint met ($p = 0.003$)
- Significant age by treatment interaction
  - ~1/3 of children treated with 250 µg were able to tolerate > 1,000 mg protein (~4 peanuts)
  - Significant increase in IgG4

Viaskin Milk Phase II Program: MILES
Viaskin Milk: Milk Allergy (CMPA) Phase II Study
Identified Safe/Effective Dose for Children

**Clinical Trial Patient Population**
- Children (2-11) and adolescents (12-17)
- Highly sensitive to milk (≥ 10 kU/L milk-specific IgE and ≥ 6 mm SPT* wheal)
- Reactive dose at baseline (M0) ≤300 mg of cow’s milk protein (CMP) (~ ≤ 9.4 mL of cow’s milk)

**Efficacy Endpoints**
- **Treatment responder definition at M12:**
  - ≥ 10-fold increase in CRD** and at least 144 mg of CMP
  - OR CRD ≥ 1,444 mg
- **Key secondary endpoints:**
  - Change from baseline in IgE, IgG4

---

*SPT: Skin Prick Test
**CRD: Cumulative Reactive Dose at Food Challenge
***Protocol change implemented in August 2018 to switch all patients to 300 µg (from 500 µg) for treatment up to 24 months

Denotes a completed food challenge; Denotes a pending, optional food challenge
**MILES Patient Population at Baseline**

198 patients randomized
- 152 Children (2-11)
- 46 Adolescents (12-17)

**CRD of Cow’s Milk**

**Mean**
- Children: 216.3 mg
- Adolescents: 222.0 mg

**Median**
- Children: 144 mg
- Adolescents: 144 mg

**Medical history of patients**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>139</td>
<td>70.2</td>
</tr>
<tr>
<td>Atopic Dermatitis</td>
<td>139</td>
<td>70.2</td>
</tr>
<tr>
<td>Allergic Rhinitis</td>
<td>144</td>
<td>72.7</td>
</tr>
<tr>
<td>Polyallergic</td>
<td>178</td>
<td>89.9</td>
</tr>
</tbody>
</table>

**Mean Cow’s Milk sIgE**

- Children: 135.2 kU/L
- Adolescents: 127.9 kU/L
MILES Results: Support Viaskin Milk 300µg as the Potential First Treatment for CMPA in Children 2-11

Favorable safety, tolerability and compliance

- Overall discontinuation rate of 4.5%
  - 1.5% dropout due to AEs
- Most AEs related to application site (mild to moderate)
- No severe anaphylaxis
- No SAEs or epinephrine related to treatment
- Treatment adherence was high
  - Mean patient compliance > 95%

Response Rate (ITT*)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% of Responders (90% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>32.5%</td>
</tr>
<tr>
<td>150 µg</td>
<td>34.2%</td>
</tr>
<tr>
<td>300 µg</td>
<td>57.9%</td>
</tr>
<tr>
<td>500 µg</td>
<td>38.9%</td>
</tr>
</tbody>
</table>

* Missing data: failure imputation (considered as non-responders) in ITT population
P-values obtained using exact logistic regression

ITT, Intent-to-Treat
MILES Results: Significant Improvement in Threshold Reactivity with Viaskin Milk 300µg in Children 2-11

Change of CRD (ITT*)

- Placebo: 565.6 (SE 120, n = 39) \( p = 0.822 \)
- VM150 µg: 624.6 (SE 300, n = 37) \( p = 0.043 \)
- VM300 µg: 1322.4 (SE 100, n = 36) \( p = 0.985 \)
- VM500 µg: 839.8 (SE 62, n = 34) \( p = 0.617 \)

Change of CRD (PP*)

- Placebo: 510.8 (SE 100, n = 35) \( p = 0.985 \)
- VM150 µg: 569.6 (SE 106, n = 28) \( p = 0.045 \)
- VM300 µg: 1340.3 (SE 100, n = 32) \( p = 0.809 \)
- VM500 µg: 848.0 (SE 25, n = 32) \( p = 0.043 \)

Among patients with evaluable CRD assessment at Month 12.

Note, not all subjects underwent a Month-12 OFC: 1 subject in PBO, 1 subject in VM150 µg, 2 in VM300 µg, and 2 in VM500 µg did not report Month-12 CRD.

P-values obtained from ANCOVA model including on CRD at M0 and treatment group as fixed effect, using log-transformed data.
MILES Results: All Dose Cohorts At Month-12 Response Rate, Overall Population (ITT*)

**Response Rate (ITT*)**

- Placebo: 30.2% (n = 53)
- VM150 µg: 36.7% (n = 49)
- VM300 µg: 49.0% (n = 49)
- VM500 µg: 36.2% (n = 47)

P-values obtained using exact logistic regression:
- Placebo vs. VM150 µg: p = 0.682
- Placebo vs. VM300 µg: p = 0.085
- Placebo vs. VM500 µg: p = 0.641

**Response Rate (PP)**

- Placebo: 28.9% (n = 45)
- VM150 µg: 36.1% (n = 36)
- VM300 µg: 55.0% (n = 40)
- VM500 µg: 37.2% (n = 43)

P-values obtained using exact logistic regression:
- Placebo vs. VM150 µg: p = 0.522
- Placebo vs. VM300 µg: p = 0.027
- Placebo vs. VM500 µg: p = 0.649

*Missing data: failure imputation (considered as non-responders) in ITT population

P-values obtained using exact logistic regression

ITT=Intent-to-Treat; PP=Per Protocol
MILES Results: All Dose Cohorts At Month-12 CRD, Overall Population (ITT)

<table>
<thead>
<tr>
<th>Dose Cohort</th>
<th>CRD Increase at M12 vs Baseline, mg*</th>
<th>Median CRD Increase</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>555.5</td>
<td>100 mg</td>
<td>39</td>
</tr>
<tr>
<td>150 µg</td>
<td>745.1</td>
<td>300 mg</td>
<td>37</td>
</tr>
<tr>
<td>300 µg</td>
<td>1,201.0</td>
<td>400 mg</td>
<td>36</td>
</tr>
<tr>
<td>500 µg</td>
<td>723.5</td>
<td>93 mg</td>
<td>34</td>
</tr>
</tbody>
</table>

*p = 0.736

*p = 0.008

*p = 0.189

*Among patients with evaluable CRD assessment at Month 12

†Note, not all subjects underwent a Month-12 OFC: 1 subject in PBO, 1 subject in VM150 µg, 4 in VM300 µg, and 2 in VM500 µg did not report Month-12 CRD

P-values obtained from ANCOVA model including CRD at M0 and treatment group as fixed effect, using log-transformed data

ITT=Intent-to-Treat; PP=Per Protocol; SE=Standard Error
MILES Immunologic Data in Children 2-11 (ITT): Significant Immunomodulation with Viaskin Milk

• For sIgE levels in children, there is a trend towards reduction with VM doses
• No changes observed in SPT responses

P-values obtained from repeated-measures ANCOVA model including treatment group, timepoint, treatment-by-timepoint interaction and M0 value as fixed effect, using log-transformed data; ITT=Intent-to-Treat
MILES Immunologic Data in Children 2-11 (ITT): Significant Immunomodulation with Viaskin Milk

- There is a trend towards reduction of sIgE levels in VM doses

P-values obtained from repeated-measures ANCOVA model including treatment group, timepoint, treatment-by-timepoint interaction and M0 value as fixed effect, using log-transformed data; ITT=Intent-to-Treat