Aimmune's PALISADE-ARC004 Longitudinal Study Showed PALFORZIA® Safety and Efficacy Increased Over Time in Patients with Peanut Allergy

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— Findings Published in Allergy the Official Journal of the European Academy of Allergy and Clinical Immunology Demonstrated Daily Dosing Beyond 1 Year Led to Improved Safety and Tolerability —

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After 2 Years of Daily Treatment, More than 80% of Patients Were Successfully Desensitized to 2000 mg of Peanut Protein Compared to Less than 50% of the Patients Who Completed ~1.5 Years of Treatment —

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Results Suggest Clinically Meaningful Improvements in Food Allergy-Related Quality of Life Associated with Increased Desensitization

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BRISBANE, Calif.--(BUSINESS WIRE)-- Aimmune Therapeutics, Inc., a Nestlé Health Science company developing and commercializing pharmaceutical therapies to prevent, manage, and treat food and metabolic-related diseases, today announced the publication of a longitudinal analysis that explored the safety, efficacy and food allergy-related quality of life of long-term treatment with PALFORZIA® [Peanut (*Arachis hypogaea*) Allergen Powder-dnfp, previously known as investigational agent AR101] in patients with peanut allergy. The data were published in *Allergy,*the official journal of the European Academy of Allergy and Clinical Immunology (EAACI).

The analysis showed that peanut-allergic patients ages 4 through 17 who continued daily maintenance with PALFORZIA for up to two years were able to tolerate higher doses of peanut during the food exit challenge. Furthermore, the analysis showed consistent tolerability with a decrease in the frequency of adverse events (AEs) over time, as well as improvements in food-allergy related quality of life with increased duration of treatment. Adverse events in the study were mostly mild-to-moderate, with low rates of serious/severe AEs and AE-related treatment discontinuations.

The manuscript, titled "
Open-label follow-on study evaluating the efficacy, safety, and quality of life with extended daily oral immunotherapy in children with peanut allergy,
" was published online.

"As the first FDA-approved oral immunotherapy for peanut allergy, PALFORZIA represents an important advance in the management of this debilitating food allergy that is associated with constant vigilance and stress for both children and their families," said Louise Peacock, Global Head of Research and Development for Aimmune Therapeutics. "The long-term data from this analysis reinforce that ongoing treatment with PALFORZIA can help reduce that burden and improve the quality of life of patients and their caregivers, while also continuing to increase desensitization to peanut protein over time with fewer adverse events. We are encouraged by these results and committed to gathering additional data to help assess the benefits of PALFORZIA in a real-world setting."

Patients who completed the PALISADE trial were eligible to enter the ARC004 open-label follow-on study, which evaluated the long-term efficacy and safety of daily PALFORZIA dosing beyond one year (52 weeks). The PALISADE-ARC004 longitudinal analysis of patient data from the start of PALISADE through the end of ARC004 was designed to assess if efficacy and tolerability of daily treatment with PALFORZIA improved over time, approximately for 28 weeks (Group A) or 56 weeks (Group B) accounting for a total 1.5-2 years of treatment, as well as to evaluate the effects of PALFORZIA on patient quality of life. Safety analyses included the incidence of treatment-emergent AEs (TEAEs), both related and unrelated, including serious AEs, during the overall study period (from entry into PALISADE to exit from ARC004). Other safety measures included the incidence of systemic allergic reactions; use of adrenaline as a rescue medication; AEs leading to discontinuation; gastrointestinal (GI) AEs of clinical interest and accidental food allergen exposure. Throughout the study, a total of 10.6% of participants presented with treatment-related systemic AEs in the form of allergic reactions, two of which were considered severe (anaphylaxis) and one of which led to the discontinuation of one participant. Most AEs reported during the study requiring treatment with adrenaline were considered mild to moderate and occurred in 4.5% to 12.5% of participants across groups and dosing periods.

"The PALISADE-ARC004 results demonstrated that more than 80% of patients in the study – 21 out of 26 patients – were able to reach and tolerate a daily maintenance dose of 2000 mg (the equivalent of eight peanuts) of peanut protein after two years of PALFORZIA treatment. This is a much higher dose than 125 mg, which is known to cause reactions with accidental peanut exposure in certain untreated individuals," continued Peacock.

Key PALISADE-ARC004 findings include:

- After two years of daily PALFORZIA treatment, 80.8% of study participants tolerated 2000 mg of peanut protein in the double-blind, placebo-controlled food challenge.
- The total number of treatment emergent adverse events decreased during the course of the intervention period (PALISADE and ARC2004) in groups that received 300 mg of PALFORZIA for both 1.5 and 2 years from 56.6% percent to 12.8% and 82.7% to 17.5%, respectively.
- Changes from baseline in immune markers (peanut specific IgE and IgG levels) with continued PALFORZIA treatment demonstrated ongoing immunomodulation during the first two years of treatment. IgE levels decreased from the time of PALISADE entry to ARC004 exit, whereas IgG4 levels increased.
    - Reductions were observed in the ratio of peanut specific IgE/IgG4 from screening to ARC004 exit.
    - Mean peanut SPT wheal diameters decreased from screening to ARC004 exit, with the most important reduction after up-dosing.
- The Food Allergy Quality of Life Questionnaire (FAQLQ) and Food Allergy Independent Measure (FAIM) at PALISADE screening (before the entry double-blind, placebo-controlled food challenge (DBPCFC)), at PALISADE exit/ARC004 screening (after the DBPCFC and unblinding), and after the exit ARC004 DBPCFC, demonstrate:
    - The percentage of children and teenagers demonstrating clinically meaningful improvement in the FAQLQ total and domain scores (≥0.5) generally rose with the duration of PALFORZIA treatment.

- The percentage of caregiver documented meaningful improvements in FAQLQ total and domain scores (≥0.5) of their children (aged 7-12) and teenagers (aged 13-17) increased progressively from PALISADE baseline to ACR004 exit.

PALFORZIA was approved by the U.S. Food and Drug Administration (FDA) in January 2020 as an oral immunotherapy for the mitigation of allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanut in patients aged 4 through 17 years with a confirmed diagnosis of peanut allergy. In December 2020, the European Commission (EC) approved PALFORZIA for patients aged 4 to 17 years with a confirmed diagnosis of peanut allergy in conjunction with a peanut-avoidant diet.

About PALISADE-ARC004

PALISADE-ARC004

PALISADE-ARC004 aimed to explore the impact of continued PALFORZIA therapeutic maintenance dosing (300 mg/day) on efficacy, safety/tolerability, and food allergy-related quality of life. This analysis focuses on a subset of PALISADE participants who completed treatment with PALFORZIA, tolerated ≥300 mg peanut protein (443 mg cumulative) at PALISADE exit double-blind, placebo-controlled food challenge (DBPCFC), and enrolled in ARC004. Participants received daily therapeutic maintenance dosing (300mg/day) for 28 weeks (Group A) or 56 weeks (Group B) accounting for a total of ~1.5 and 2 years of treatment respectively including PALISADE. This analysis included 142 participants ages 4–17 years. Two participants in these cohorts turned 18 during PALISADE and were included in this analysis but not in the ARC004 analyses. Safety measures included the incidence of systemic allergic reactions; use of adrenaline as a rescue medication; AEs leading to discontinuation; gastrointestinal (GI) AEs of clinical interest including abdominal pain, and accidental food allergen exposure.

About ARC004

ARC004 was an open-label follow-on study to the phase 3 PALISADE trial and assessed the safety and efficacy of extended daily and non-daily dosing of PALFORZIA across 351 peanut-allergic patients ages 4 to 17 years. Participants who received placebo (PALFORZIA-naïve) in PALISADE received active treatment with PALFORZIA, and eligible participants who received PALFORZIA in PALISADE (PALFORZIA continued) were assigned to either daily or non-daily continued treatment regimen with different durations. A total of 261 PALFORZIA-treated participants completed the ARC004 study.

About PALISADE

PALISADE (Peanut Allergy oral Immunotherapy Study of AR101 for Desensitization) was an international, randomized (3:1), double-blind, placebo-controlled, phase 3 trial to evaluate the efficacy and safety of AR101 in patients with peanut allergy. PALISADE was conducted at 66 sites in 10 countries in North American and Europe, where 496 patients ages 4–17 received either AR101 or placebo (372 AR101, 124 placebo), along with 55 adults ages 18–49, who were not part of the primary analysis. To meet PALISADE's inclusion criteria, patients could tolerate no more than the 30-mg dose of peanut protein in an entry double-blind, placebo-controlled food challenge (DBPCFC), which consisted of consecutive doses of 1, 3, 10, 30 and 100 mg of peanut protein, given 20 to 30 minutes apart, as tolerated with no more than mild symptoms. Patients enrolled in PALISADE underwent a dose escalation period of approximately 22 weeks to reach a maintenance dose of 300 mg per day of AR101 or placebo, then continued with daily maintenance at 300 mg per day of AR101 or placebo for approximately six months. At that point, patients underwent an exit DBPCFC, which tested consecutive doses of 3, 10, 30, 100, 300, 600 and 1,000 mg of peanut protein, given 20 to 30 minutes apart, as tolerated with no more than mild symptoms. Both the entry and exit DBPCFCs used an independent, blinded assessor. Following the completion of the exit DBPCFC, patients were unblinded and eligible to rollover or crossover into the follow-on ARC004 clinical trial, as appropriate.

INDICATION

PALFORZIA is an oral immunotherapy indicated for the mitigation of allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanut. PALFORZIA is approved for use in patients with a confirmed diagnosis of peanut allergy. Initial Dose Escalation may be administered to patients aged 4 through 17 years. Up-Dosing and Maintenance may be continued in patients 4 years of age and older.

PALFORZIA is to be used in conjunction with a peanut-avoidant diet.

Limitations of Use: Not indicated for the emergency treatment of allergic reactions, including anaphylaxis.

IMPORTANT SAFETY INFORMATION

Boxed WARNING:

PALFORZIA can cause anaphylaxis, which may be life threatening and can occur at any time during PALFORZIA therapy.

Prescribe injectable epinephrine, instruct and train patients on its appropriate use, and instruct patients to seek immediate medical care upon its use.

Do not administer PALFORZIA to patients with uncontrolled asthma.

Dose modifications may be necessary following an anaphylactic reaction.

Observe patients during and after administration of the Initial Dose Escalation and the first dose of each Up-Dosing level, for at least 60 minutes.

PALFORZIA is available only through a restricted program called the PALFORZIA REMS.

CONTRAINDICATIONS

PALFORZIA is contraindicated in patients with uncontrolled asthma, or with a history of eosinophilic esophagitis and other eosinophilic gastrointestinal disease.

WARNINGS AND PRECAUTIONS

Anaphylaxis

PALFORZIA can cause anaphylaxis, which may be life threatening. PALFORZIA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the PALFORZIA REMS because of the risk of anaphylaxis. Only prescribers, healthcare settings, pharmacies, and patients certified and enrolled in the REMS Program can prescribe, receive, dispense or administer PALFORZIA.

Anaphylaxis has been reported during all phases of PALFORZIA dosing, including Maintenance and in subjects who have undergone recommended Up-Dosing and dose modification procedures.

Do not initiate PALFORZIA treatment in a patient who has had severe or life-threatening anaphylaxis within the previous 60 days. PALFORZIA may not be suitable for patients with certain medical conditions that may reduce the ability to survive anaphylaxis, including but not limited to markedly compromised lung function, severe mast cell disorder, or cardiovascular disease. In addition, PALFORZIA may not be suitable for patients taking medications that can inhibit or potentiate the effects of epinephrine.

All Initial Dose Escalation doses and the first dose of each Up-Dosing level must be administered in a certified health care setting.

Patients may be more likely to experience allergic reactions following PALFORZIA administration in the presence of cofactors such as exercise, hot water exposure, intercurrent illness (e.g., viral infection), or fasting. Other potential cofactors may include menstruation, sleep deprivation, nonsteroidal anti-inflammatory drug use, or uncontrolled asthma. Patients should be proactively counseled about the potential for the increased risk of anaphylaxis in the presence of these cofactors. If possible, adjust the time of dosing to avoid these cofactors. If it is not possible to avoid these cofactors, consider withholding PALFORZIA temporarily.

Asthma

Uncontrolled asthma is a risk factor for a serious outcome, including death, in anaphylaxis. Ensure patients with asthma have their asthma under control prior to initiation of PALFORZIA.

PALFORZIA should be temporarily withheld if the patient is experiencing an acute asthma exacerbation. Following resolution of the exacerbation, resumption of PALFORZIA should be undertaken cautiously. Re-evaluate patients who have recurrent asthma exacerbations and consider discontinuation of PALFORZIA.

Eosinophilic Gastrointestinal Disease

Discontinue PALFORZIA and consider a diagnosis of eosinophilic esophagitis in patients who experience severe or persistent gastrointestinal symptoms, including dysphagia, vomiting, nausea, gastroesophageal reflux, chest pain, or abdominal pain.

Gastrointestinal Adverse Reactions

Gastrointestinal adverse reactions were commonly reported in PALFORZIA-treated subjects, and dose modification should be considered for patients who report these reactions. For severe or persistent gastrointestinal symptoms consider a diagnosis of eosinophilic esophagitis.

ADVERSE REACTIONS

The most common adverse events reported in subjects treated with PALFORZIA (incidence ≥ 5% and ≥ 5% than placebo) are abdominal pain, vomiting, nausea, oral pruritus, oral paresthesia, throat irritation, cough, rhinorrhea, sneezing, throat tightness, wheezing, dyspnea, pruritus, urticaria, anaphylactic reaction, and ear pruritus.

Please see full Prescribing Information, including Boxed WARNING, and Medication Guide at www.PALFORZIA.com.

For more information about PALFORZIA, please call 1-844-PALFORZ (1-844-725-3679) or visit www.PALFORZIA.com.

About Aimmune

Aimmune Therapeutics, Inc., a Nestlé Health Science Company, is a biopharmaceutical company developing and commercializing pharmaceutical therapies to prevent, manage, and treat food and metabolic-related diseases, including gastrointestinal conditions. Aimmune has one FDA- and EU-approved medicine for peanut allergy and other investigational therapies in development. For more information, please visit www.aimmune.com.

About Nestlé Health Science

Nestlé Health Science (NHSc), a wholly owned subsidiary of Nestlé, is a globally recognized leader in the field of nutritional science. At NHSc we are committed to empowering healthier lives through nutrition for consumers, patients and their healthcare partners. We offer an extensive consumer health portfolio of industry-leading medical nutrition, consumer and vitamins, minerals and supplements (VMS) brands that are science-based solutions covering all facets of health from prevention to maintenance, all the way through to treatment. NHSc is redefining the way we approach the management of health in several key areas such as pediatric health, allergy, acute care, oncology, metabolic health, healthy aging, gastrointestinal health, and inborn errors of metabolism. Headquartered in Switzerland, NHSc employs over 5,000 people around the world who are committed to making a difference in people's lives, for a healthier today and tomorrow. www.nestlehealthscience.com.

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