# A Novel Characterized Peanut Allergen Formulation (AR101) for Oral Immunotherapy (OIT) Induces Desensitization in Peanut-Allergic Subjects:

## *A Phase 2 Clinical Safety and Efficacy Study*

Bird JA, Spergel JM, Jones SM, Rachid R, Assa'ad AH, Wang J, Leonard SA, Laubach SS, Kim EH, Vickery BP, Davis B, Heimall J, Cinaferoni A, MacGinnitie AJ, Crestani E, Elfont RM, Sampson HA and Burks AW, The ARC001 Study Group

**EAACI Presentation by Wesley Burks, MD**
**June 7, 2015**
**Barcelona, Spain**

# Disclosure

**In relation to this presentation, I declare the following, real or perceived conflicts of interest:**

This study was sponsored by Aimmune Therapeutics


**A conflict of interest is any situation in which a speaker or immediate family members have interests, and those may cause a conflict with the current presentation. Conflicts of interest do not preclude the delivery of the talk, but should be explicitly declared. These may include financial interests (eg. owning stocks of a related company, having received honoraria, consultancy fees), research interests (research support by grants or otherwise), organisational interests and gifts.**

# Study overview

## Background

- Food allergy prevalence is increasing worldwide, including to peanut*
- Oral immunotherapy (OIT) has shown promise as treatment for a variety of food allergies, e.g., peanut, milk, and egg
- There are no approved drug products for peanut allergy

## Objectives

- Assess clinical safety of a novel characterized peanut allergen formulation (AR101)
- Demonstrate AR101's efficacy in inducing desensitization to peanut in peanut-allergic children and young adults undergoing peanut OIT

## Primary Endpoint

- Number of subjects receiving AR101 vs. placebo in the intent-to-treat (ITT) population able to reach a maintenance dose of 300 mg/d, and to tolerate a cumulative amount of peanut protein at Exit DBPCFC ≥ 443 mg with no more than mild symptoms

*JACI. 2014;133:291-307

# Study design: Inclusion / Exclusion criteria

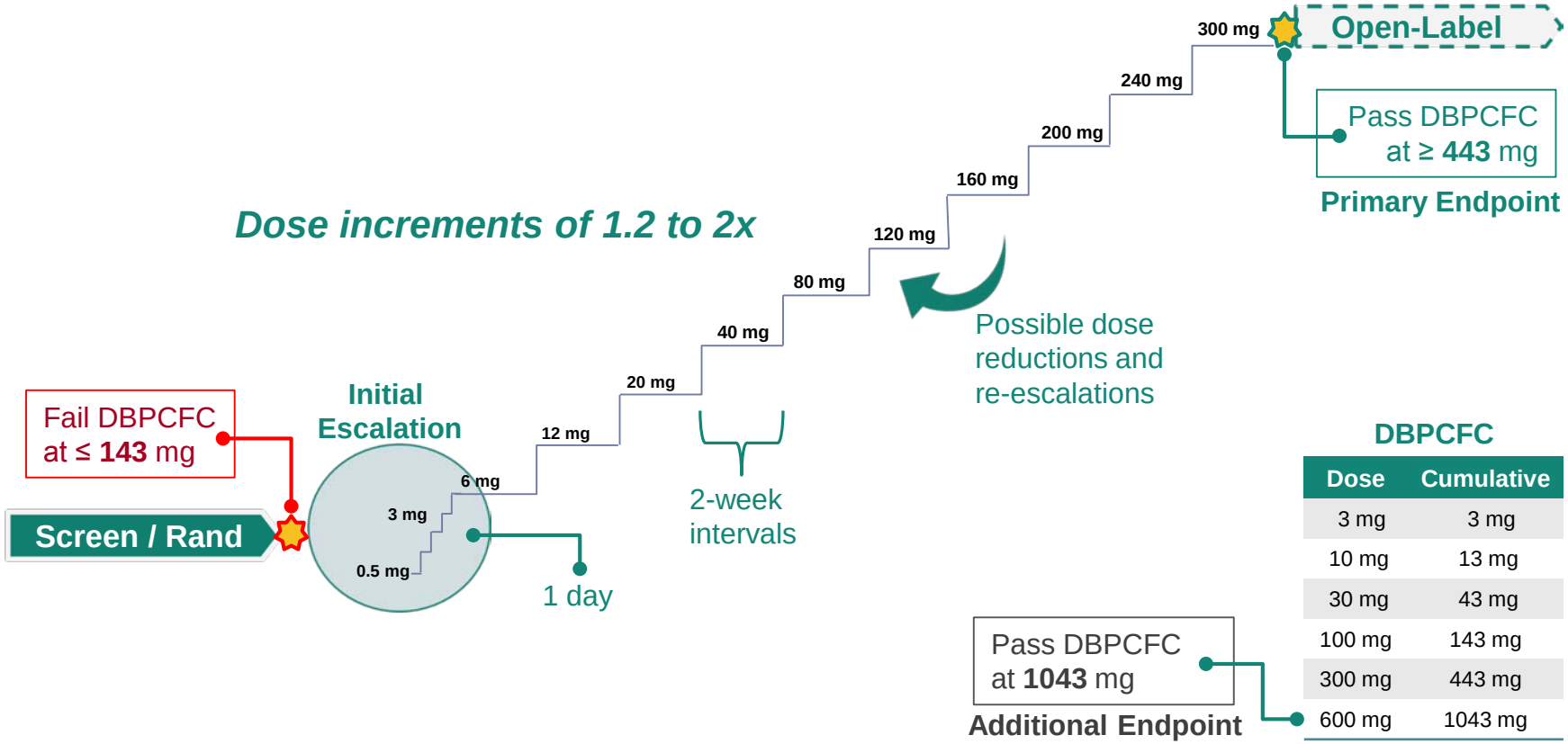
## Key Inclusion Criteria

- Ages 4 to 26 years
- History of peanut allergy
- Peanut-specific IgE > 0.35 $kU_A/L$
- Peanut skin-prick test wheal diameter > 3 mm
- Dose-limiting symptoms to ≤ 143 mg of peanut protein in DBPCFC

## Key Exclusion Criteria

- History of life-threatening anaphylaxis
- History of EGID
- Severe asthma OR mild/moderate asthma if poorly controlled

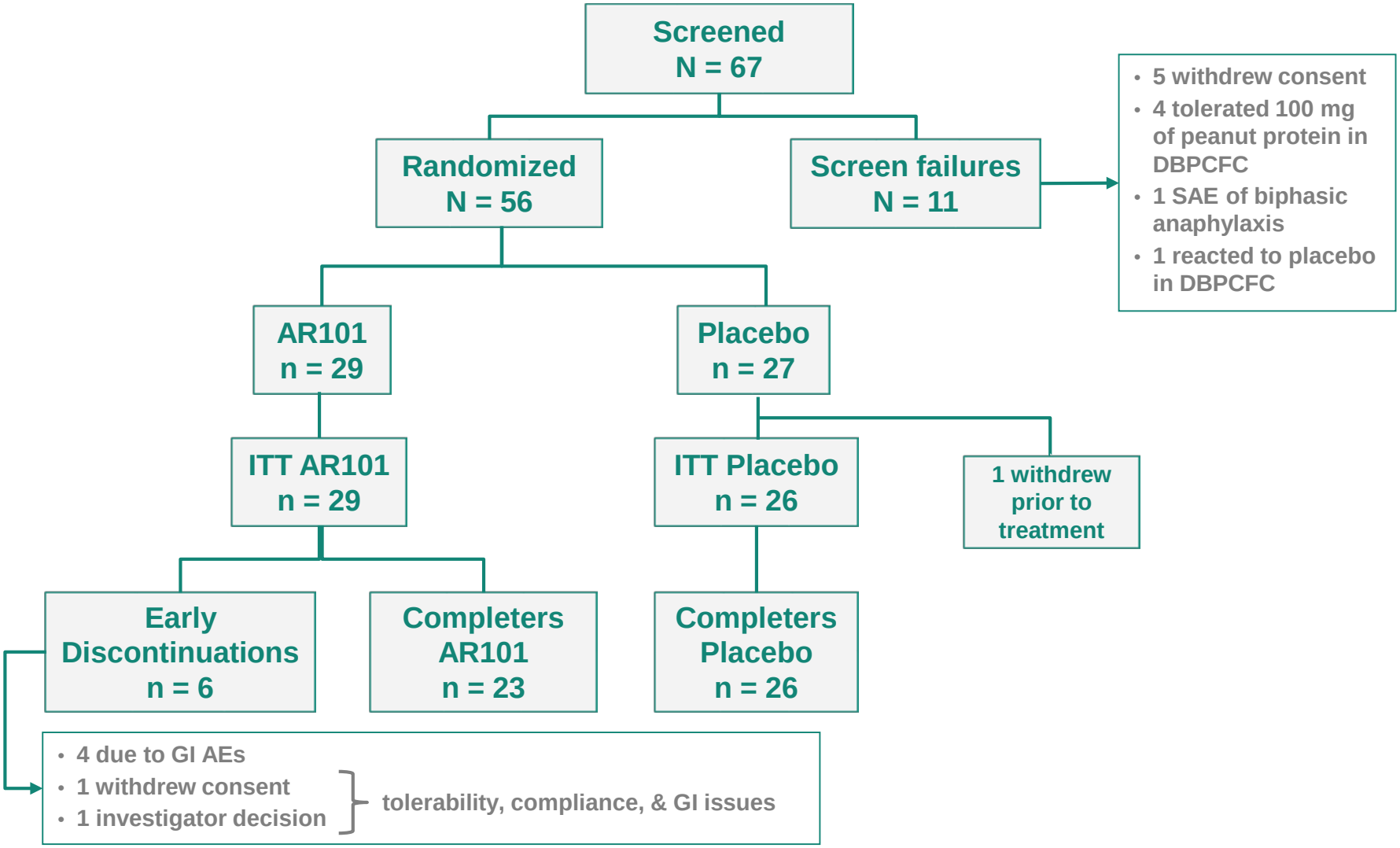
# Study design: multi-center, randomized, double-blind, placebo-controlled




**DBPCFC**

| Dose | Cumulative |
|---|---|
| 3 mg | 3 mg |
| 10 mg | 13 mg |
| 30 mg | 43 mg |
| 100 mg | 143 mg |
| 300 mg | 443 mg |
| 600 mg | 1043 mg |

# Enrollment and disposition

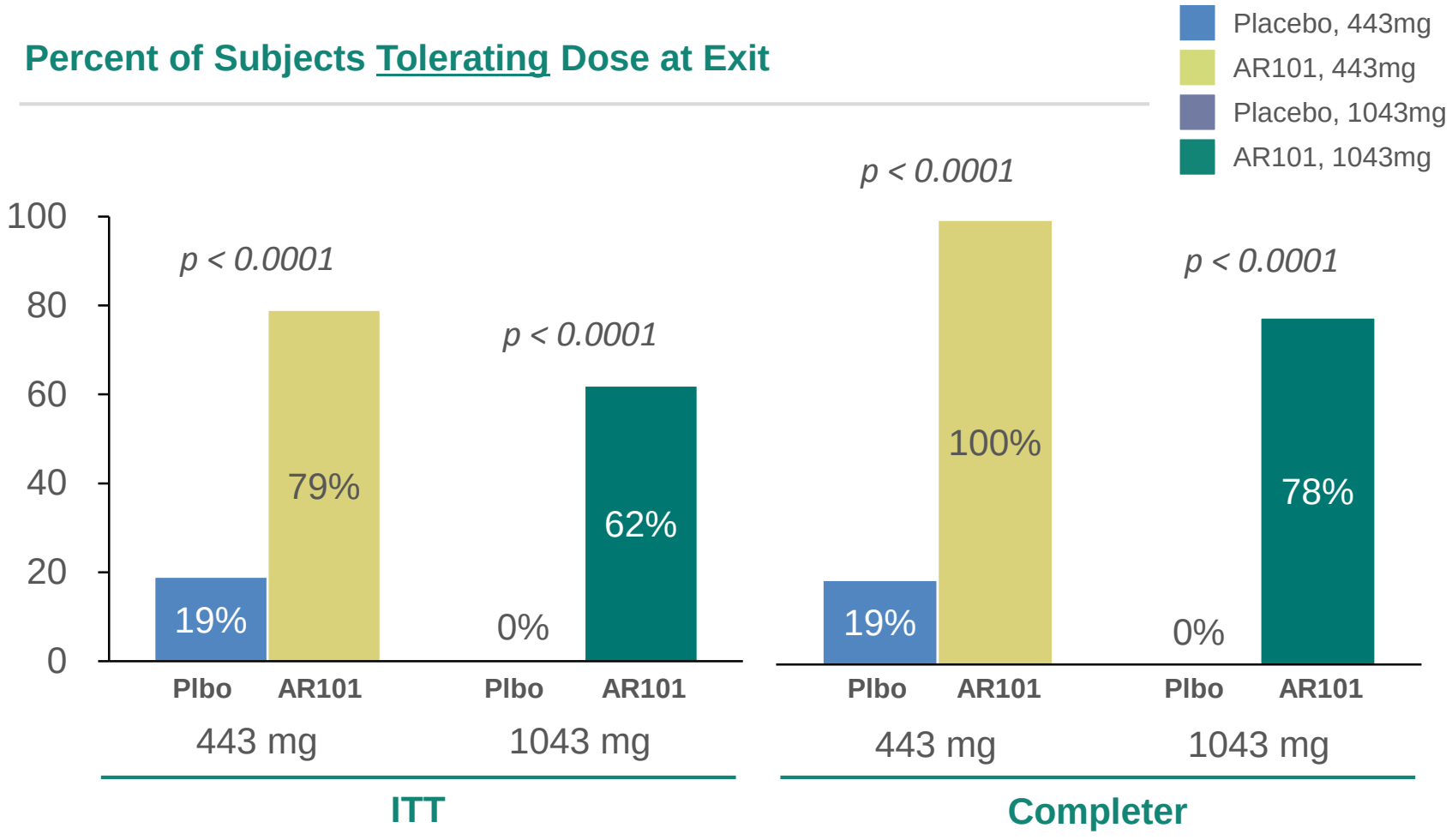


# No significant differences in demographic or baseline characteristics between treatment groups

| | Placebo | Active (AR101) |
|---|---|---|
| **n, ITT** | 26 | 29 |
| **Age,** Median (min, max) | 8 years (4 to 14) | 7 years (4 to 21) |
| **Gender** | 16 male 10 female | 20 male 9 female |
| **Peanut-specific IgE,** Median (min, max) | 100.0 (3.5 to >100) | 64.3 (0.8 to >100) |
| **Wheal,** Median (min, max) | 13 mm (5 to 26) | 14 mm (5 to 30) |
| **MTD, Cumulative,** Median (min, max) | 28 mg (3 to 30) | 13 mg (3 to 30) |

MTD = maximum tolerated dose of peanut protein in Screening DBPCFC

# Significantly more AR101 than placebo subjects tolerate top doses in the Exit DBPCFC



# Safety Overview

## Median time to reach DBPCFC: 22 weeks for both Placebo and AR101

## 6 Early Discontinuations from Active; None from Placebo

- 4 due to AEs of recurrent abdominal pain, nausea, and/or emesis
  - 1 confirmed EoE by endoscopic biopsy
- 2 due to multiple factors, including taste, compliance, and GI

- Onset of GI symptoms at 3 to 12 mg; tended to lead to early withdrawal
- Symptoms often not closely associated with time of dose administration
- Symptoms resolved within 1 to 3 weeks of AR101 discontinuation
- Consistent with previous literature reports of GI side effects with OIT

## Adverse Event Profile during OIT

- The most common treatment-related symptoms were GI: AR101 = 72%; Plbo = 27%
- 1 serious adverse event of anaphylaxis
- Only 1 epinephrine administration

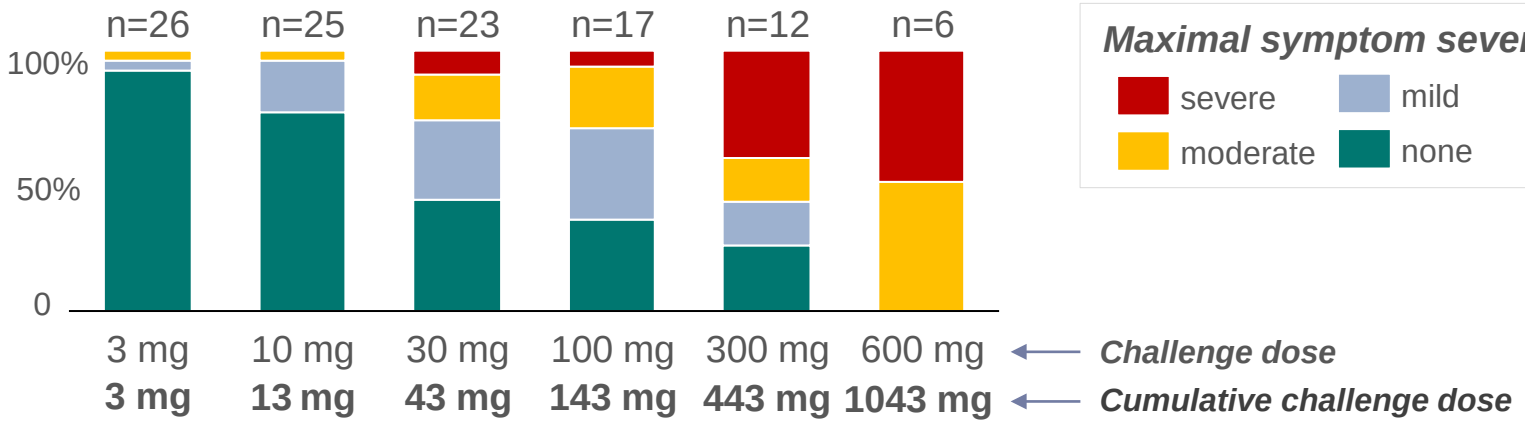
} *same subject*

- Majority of AEs graded as mild; no AEs graded as severe

*JACI. 2010;126:83-91. JACI. 2011;127:654-60, Arch Allergy Immunol. 2012;159:179-82. Lancet 2014;383:1297-304.

# Percent of completers with given symptom severity grade: less for AR101 group at each DBPCFC dose

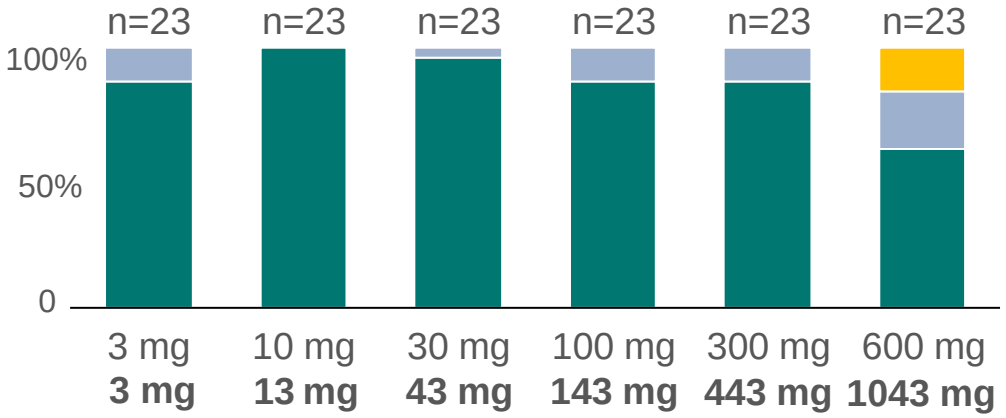
**Placebo group –** Symptom severity in exit DBPCFC




**DBPCFC reactions requiring epinephrine**

- **Placebo**: 11 subjects (3 requiring 2 injections)
- **AR101:** 2 subjects (0 requiring 2 injections)

**AR101 group –** Symptom severity in exit DBPCFC



# Summary

- AR101 had an acceptable overall safety and tolerability profile, consistent with previously reported OIT studies
- 79% of subjects tolerated up-dosing to a maintenance of 300 mg/d
- Of those who embarked on therapy (including those who discontinued prematurely), the chances of tolerating a cumulative dose of peanut protein on DBPCFC were:
  - 79% for 443 mg;
  - 62% for 1043 mg.
- For those who achieved maintenance dosing, the chances of tolerating a cumulative dose of peanut protein on DBPCFC were:
  - 100% for 443 mg;
  - 78% for 1043 mg.

# Conclusion and next steps

## Conclusion

- AR101 appears to be a safe and effective treatment option for peanut allergic individuals when used in a controlled OIT regimen

## Next Steps

- Completion of ongoing open-label follow-on study (ARC002) with an extended maintenance dosing period
- Phase 3 trial of AR101 characterized oral desensitization therapy

# Thank you for your attention

## Special thanks to our study volunteers and their families

**Thanks also to the dedicated physicians, nurses, and staff at:**

- Allergy & Asthma Medical Group, San Diego - Mary Vales and Sarah Holland
- Arkansas Children's Hospital - Denise Pearson
- Boston Children's Hospital - Heather Biehl and Sara Little
- Children's Hospital of Philadelphia - Deirdre Burke
- Children's Medical Center of Dallas - Amy Arneson
- Cincinnati Children's Hospital Medical Center - Lisa Clark
- Icahn School of Medicine at Mount Sinai - Sally Noone
- University of North Carolina School of Medicine - Jill French and Pamela Steele

*The ARC001 study was sponsored by Aimmune Therapeutics,*
*a company formerly known as Allergen Research Corporation (ARC)*

aimmune THERAPEUTICS