The Efficacy of AR101, a Peanut-Derived Pharmaceutical for Oral Immunotherapy (OIT), is Maintained and Tolerability is Increased with Low-Dose Maintenance Therapy

J. Andrew Bird, Jonathan M. Spergel, Stacie M. Jones, Rima A. Rachid, Amal H. Assa'ad, Julie Wang, Stephanie Leonard, Susan S. Laubach, Edwin H. Kim, Benjamin P. Davis, Michael J. Welch, Jennifer Heimall, Antonella Cianferoni, Andrew J. MacGinnitie, Elena Crestani, Sean R. Bennett, Brian P. Vickery, Robert M. Elfont and A. Wesley Burks, The ARC002 Study Group

UT Southwestern
Medical Center

Disclosure

This study was sponsored by Aimmune Therapeutics

Background

- Currently there is no FDA-approved therapy for peanut allergy which is rarely outgrown and prevalence is increasing,affecting >5 million patients in U.S. and EU today
- AR101 is a highly characterized, pharmaceutical-grade, peanut OIT formulation, standardized in its protein content and tested for Ara h1, h2, and h6, to provide consistent dosing of all peanut allergens
- In a previously reported double-blind, placebo-controlled Phase 2 study (ARC001), AR101 appeared to have an acceptable safety profile and desensitized 79% of subjects to 443 mg on an ITT basis and 100% of subjects on a completer basis

ARC002: An Open-label Phase 2b study

ARC002 consist of 2 parts (re-consent required between them)

- Part I – Maximum daily dose is 300 mg; efficacy and safety readouts

Objectives:

- Confirm the efficacy and safety findings of up-dosing in ARC001
- Evaluate the efficacy and safety of maintenance dosing at 300 mg/day

Endpoints:

1. Incidence of treatment-related adverse events
2. Percent of subjects desensitized during DBPCFC (post-up-dosing), defined as ingestion with no more than mild symptoms:
   - 300 mg (443 mg cumulative) of peanut protein
   - 600 mg (1043 mg cumulative) of peanut protein
   - 1000 mg (2043 mg cumulative) of peanut protein

ARC002 Inclusion / Exclusion Criteria

- Satisfied the inclusion/exclusion criteria for ARC001

Key inclusion criteria:

- Ages 4 – 26 years
- History of peanut allergy
- Peanut-specific IgE ≥0.35 kU_A/L and/or SPT ≥3 mm
- Dose-limiting symptoms to ≤143 mg of peanut protein in ARC001 Screening DBPCFC

Key exclusion criteria:

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

ARC002 Study Design: Overview

ARC001 **ARC002: Placebo Crossover Subjects**

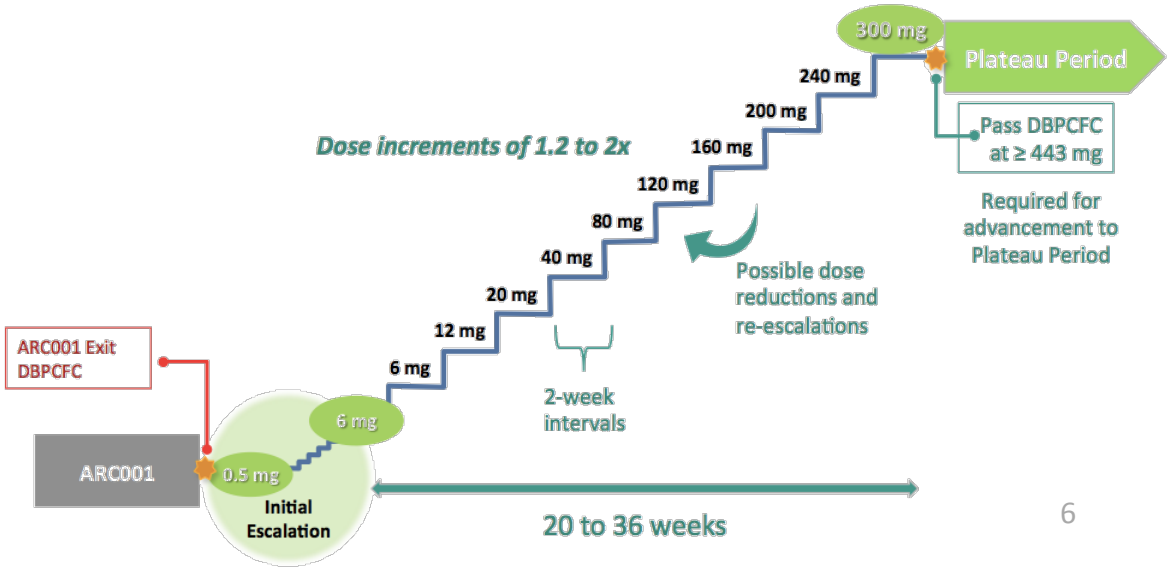
Placebo → Placebo Crossover: Up-dosing Period ~22 wks (schedule as per ARC001) → Plateau Period ~12 wks (300 mg/day) → Part 2

ARC001 **ARC002: Active Rollover Subjects**

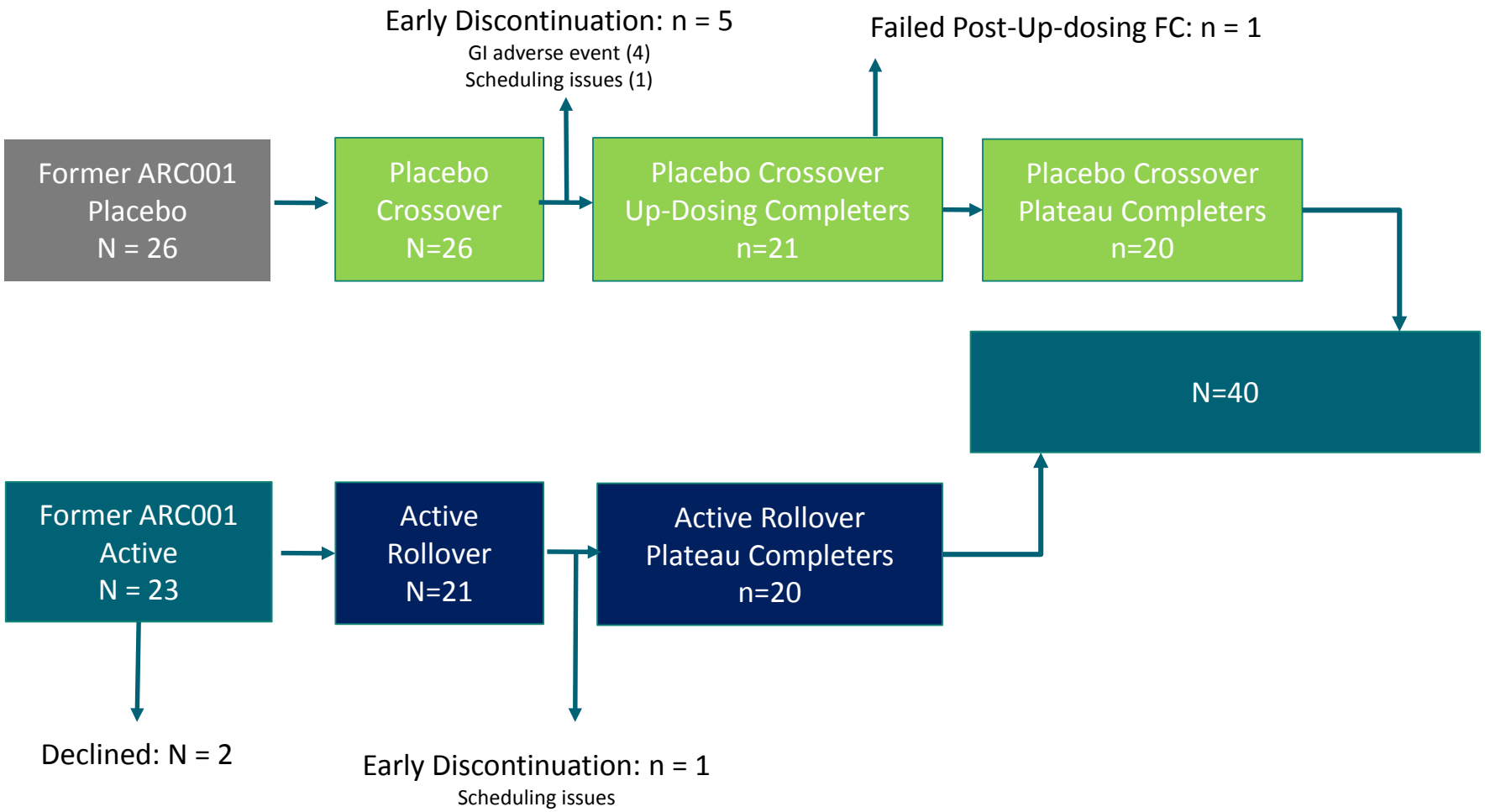
Active → Plateau Period ~12 wks (300 mg/day) → Part 2: Optional high-dose up-titration to 2000 mg and Extended Maintenance at 300 mg/d or 2000 mg/d, max.

Post-Up-dosing DBPCFC
Up to 600 mg
(1043 mg cumulative)

Post-Plateau DBPCFC
Up to 1000 mg
(2043 mg cumulative)



ARC002: Enrollment and Disposition

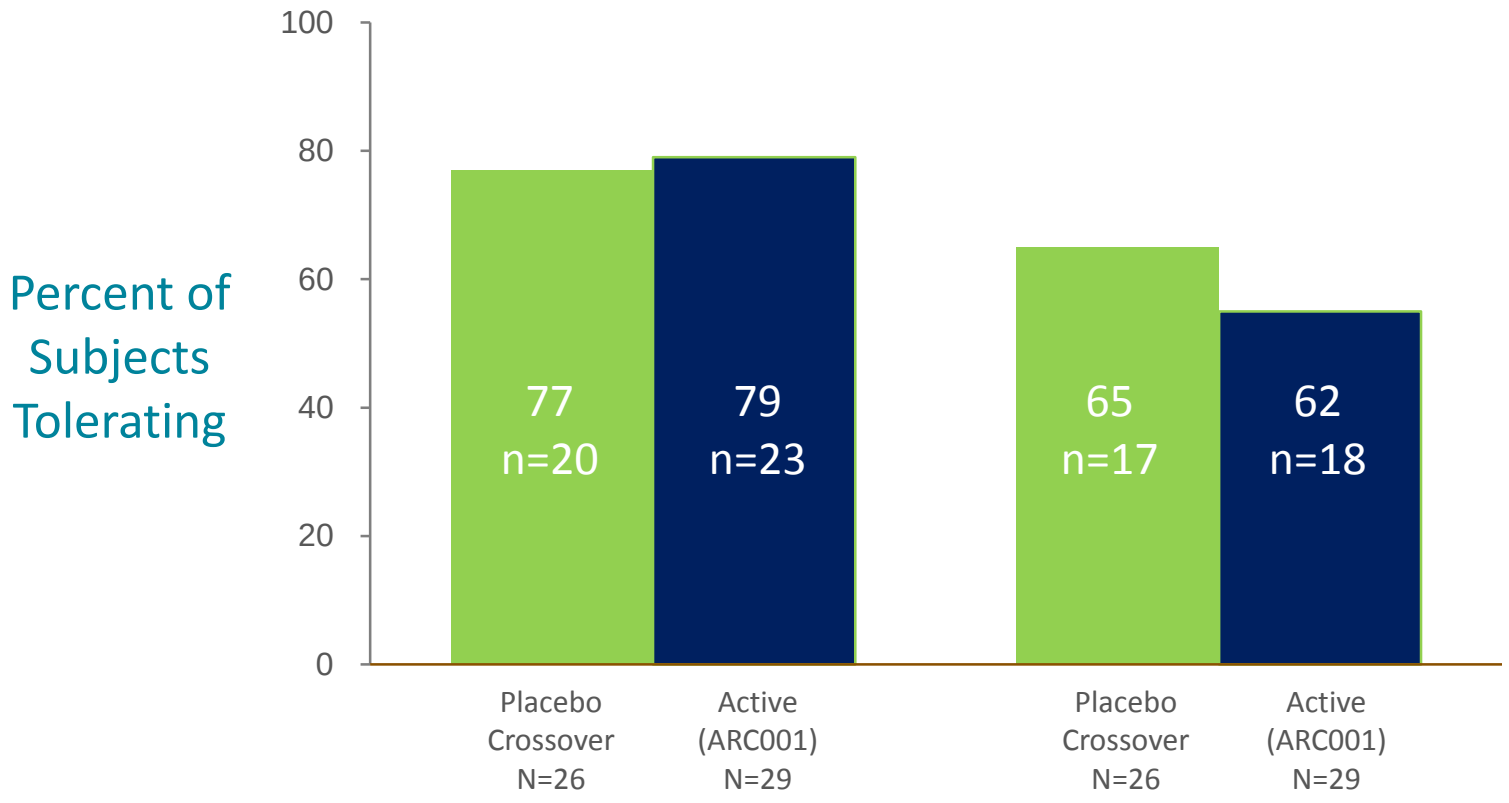


ARC002: Demographics (Safety/ITT)

	Placebo Crossover N=26	Active Rollover N=21
Age, Median (min, max)	8.5 years (5 to 14)	8.0 years (4 to 21)
Gender, n	16 male 10 female	14 male 7 female
Race, n (%)		
American Indian	1 (4)	0
Asian	1 (4)	1 (5)
Black or African-American	2 (8)	1 (5)
Pacific Islander	0	0
White	20 (77)	18 (86)
Other	2 (8)	1 (5)

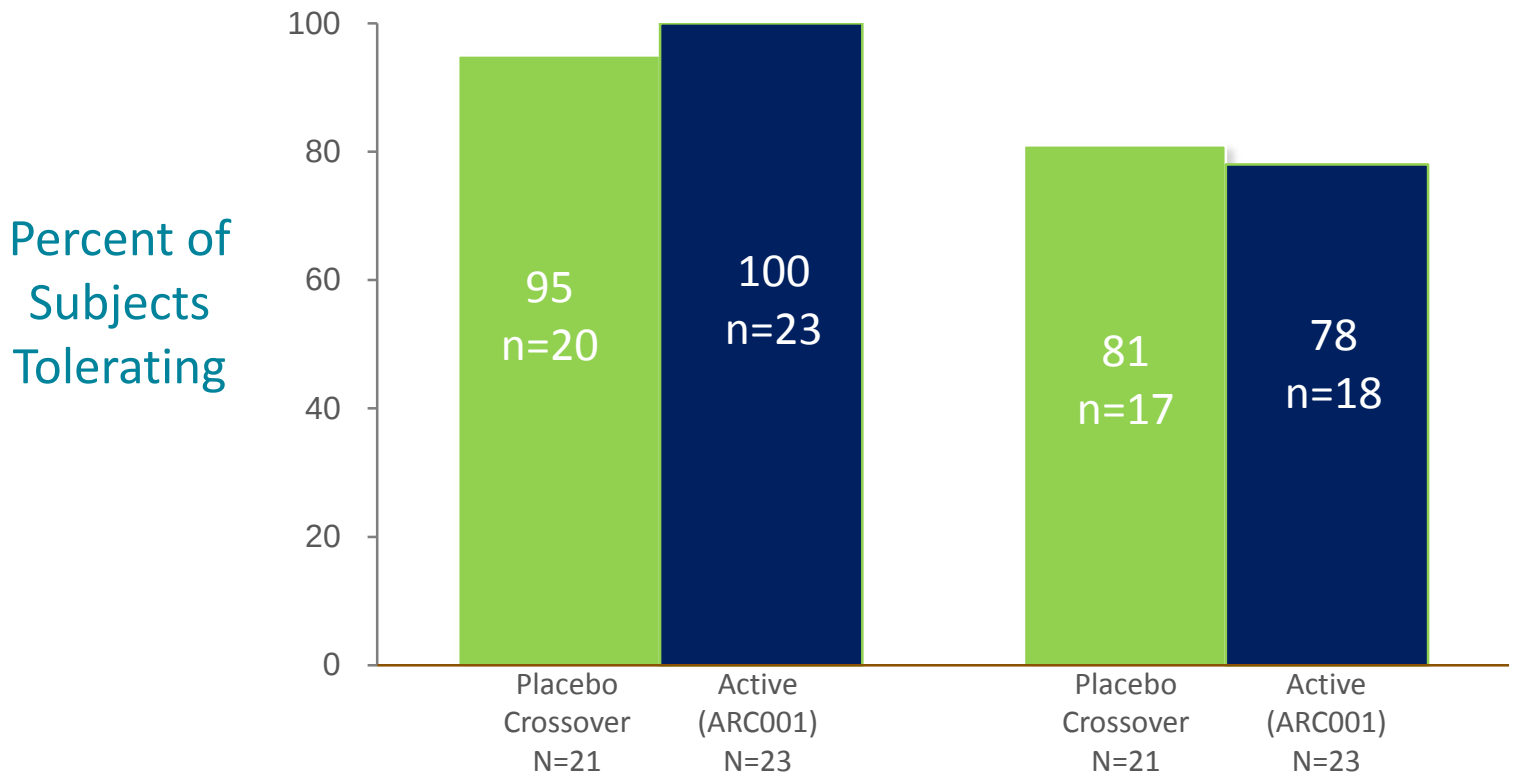
Treatment arms overall adequately balanced

Placebo Crossover Subjects Experience Similar Desensitization Rate as Active Therapy Subjects at Post-Up-dosing DBPCFC (ITT)



Challenge Dose, mg	**300**	**600**
Cumulative Dose, mg	**443**	**1043**

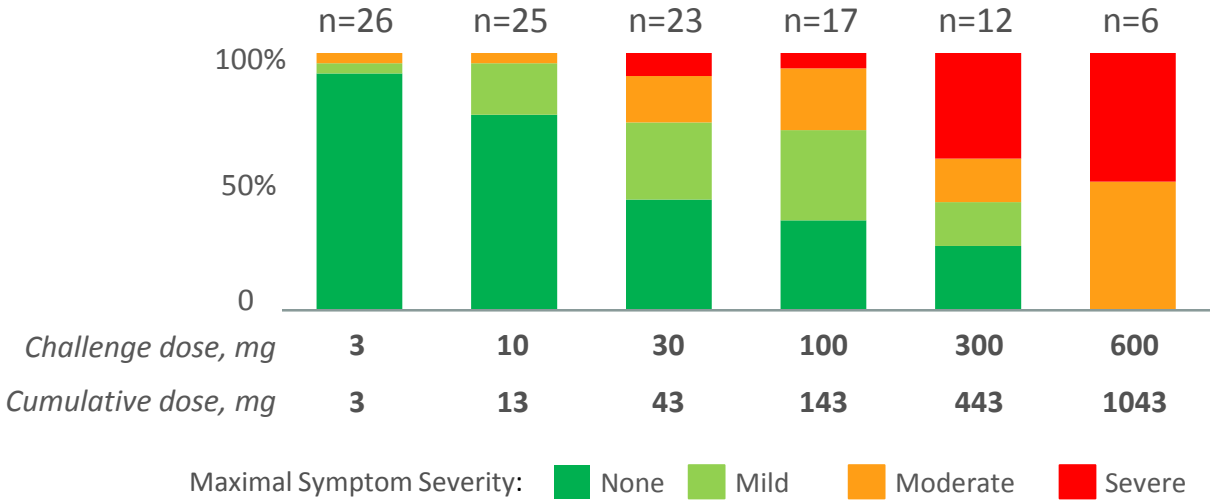
Placebo Crossover Subjects Experience Similar Desensitization Rate as Active Therapy Subjects at Post-Up-dosing DBPCFC (Completers)



Challenge Dose, mg	**300**	**600**
Cumulative Dose, mg	**443**	**1043**

AR101 Significantly Reduced Symptom Severity and Epi Use at Post-Up-Dosing DBPCFC

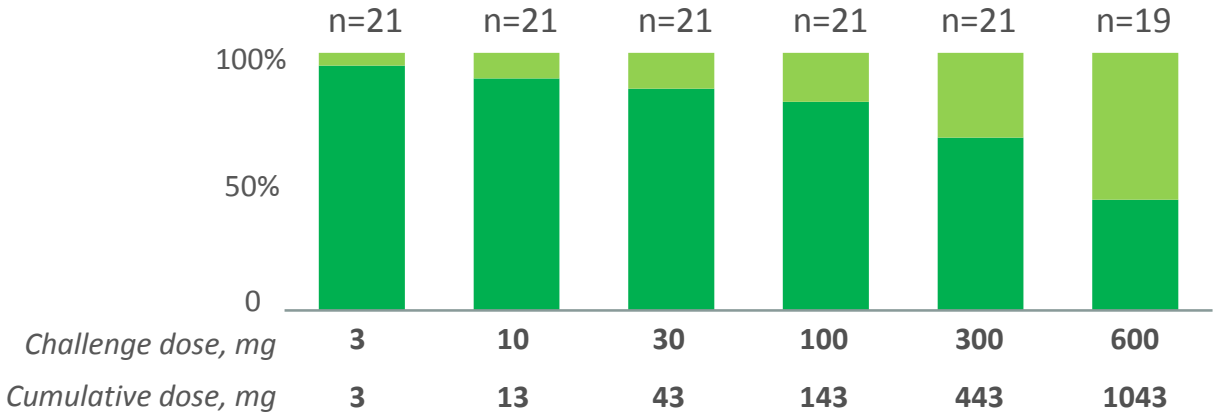
Placebo Crossover DBPCFC Symptoms Prior to Receiving AR101



Epinephrine Use by Subject:

None:	**15 (58%)**
1 injection:	**8 (31%)**
2 injections:	**3 (12%)**

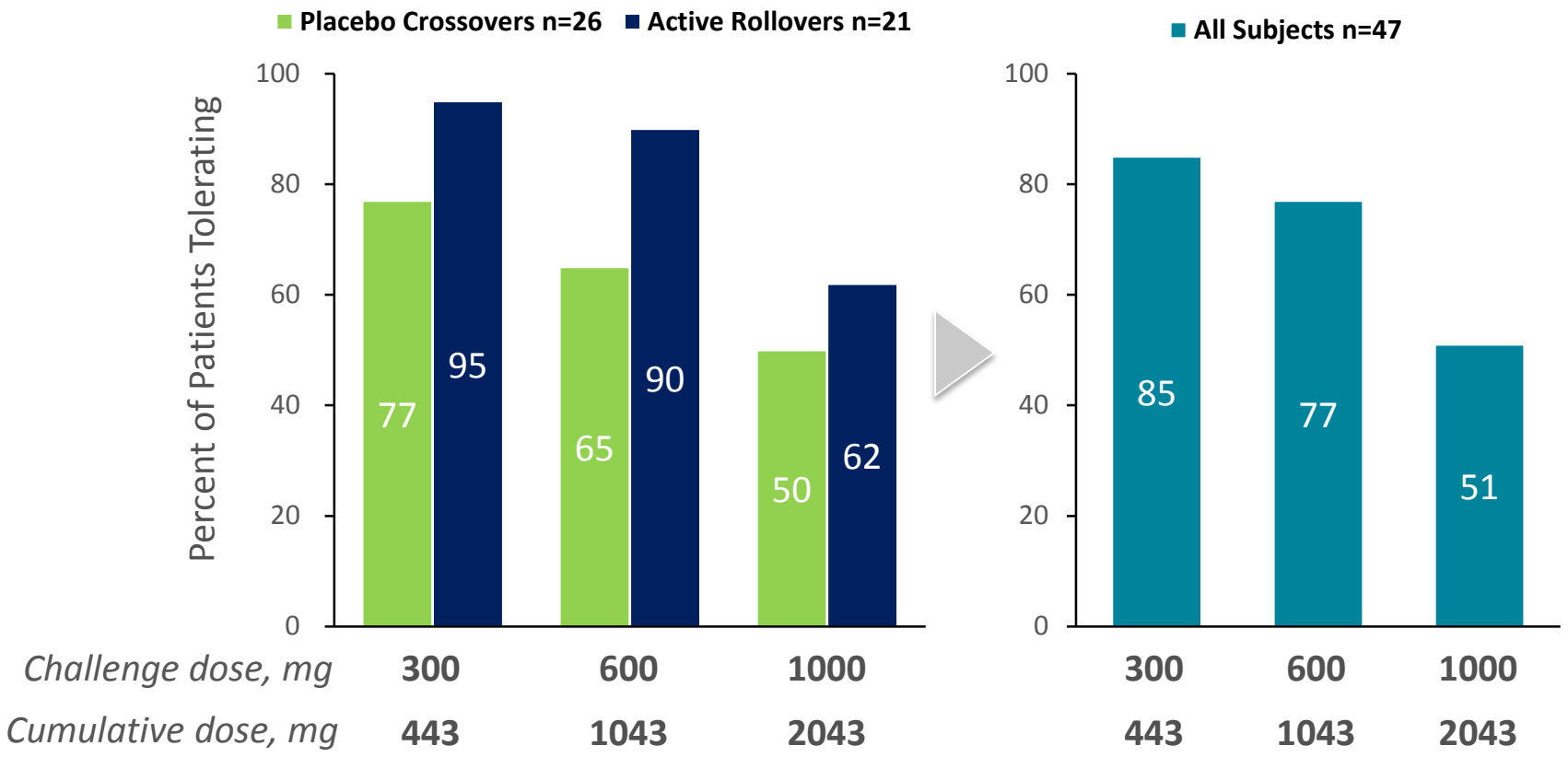
Placebo Crossover DBPCFC Symptoms AFTER AR101 Up-dosing



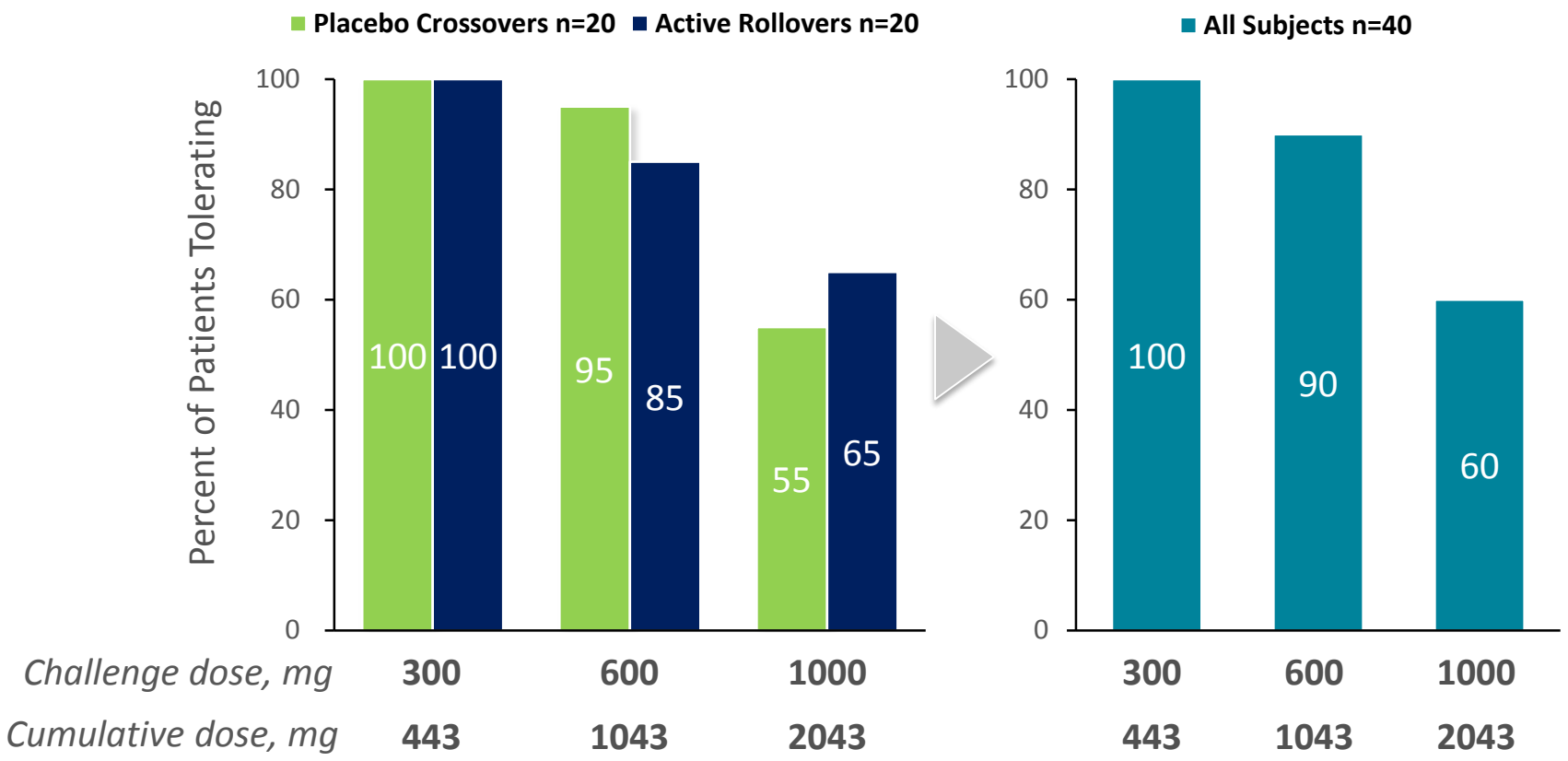
Epinephrine Use by Subject:

None:	**21 (100%)**
1 injection:	**0**
2 injections:	**0**

Desensitization Is Maintained at the Post-Plateau FC in Both Groups (ITT)



Desensitization Is Maintained at the Post-Plateau FC in Both Groups (Completers)



Safety: Numbers of subjects with AEs during 3-month Plateau Period reduced compared with Up-dosing Period

	Placebo Crossovers: N=26	
Treatment Period:	**Up-Dosing**	**Plateau**
Subjects with any AE, n (%)	25 (96)	9 (45)
Mild	12 (46)	6 (30)
Moderate	12 (46)	3 (15)
Severe	1 (4)*	0
Treatment Related AE	19 (73)	4 (20)
AE leading to discontinuation	3 (12)†	0
Anaphylaxis (non-SAE)	1 (4)‡	0
SAE	0	0

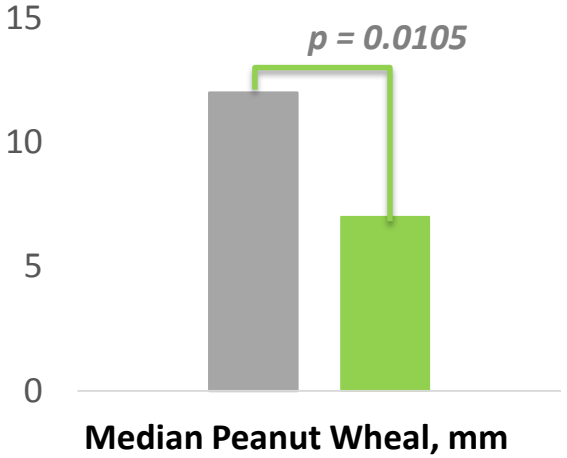
*Unrelated to treatment, AE of gastroenteritis
†All involving GI AEs
‡mild anaphylaxis at 80 mg, subject completed up-dosing

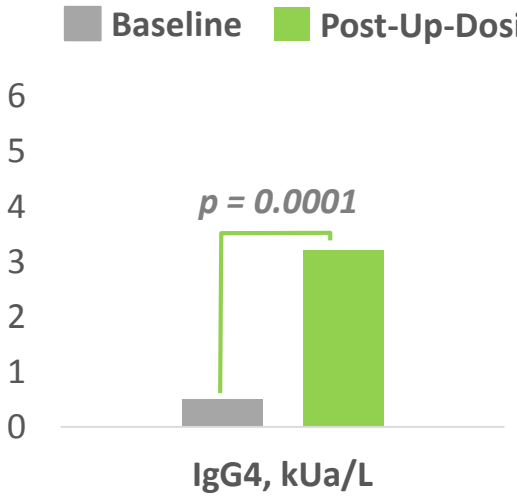
Placebo Crossovers: Safety in Up-Dosing vs Plateau (Exposure-Adjusted)

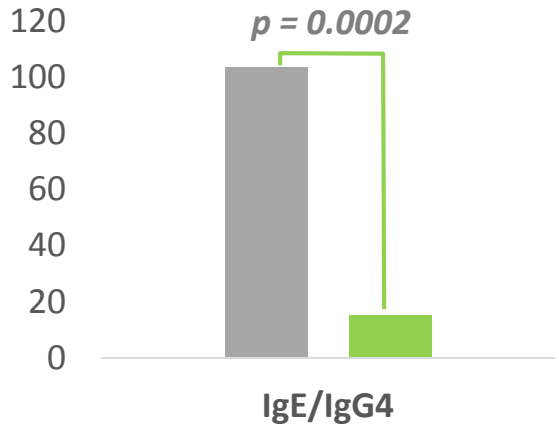
Treatment Period: (Total Subject·Days)		Placebo Crossovers N = 26 Up-Dosing (3749)	Plateau (1882)	Percent Reduction
Exposure-Adjusted AE Incidence or Events per Subject·Day	Adverse Event	0.0568	0.0154	73% ↓
	Severe AE	0.0003	0	100% ↓
	Related AE	0.0323	0.0058	82% ↓
	Related Severe AE	0	0	n/a

SPT Wheal Diameter, Increases in IgG4 and Decreases in IgE/IgG4 Ratio Were Similar Between Placebo Crossovers and Active Subjects (Completers)

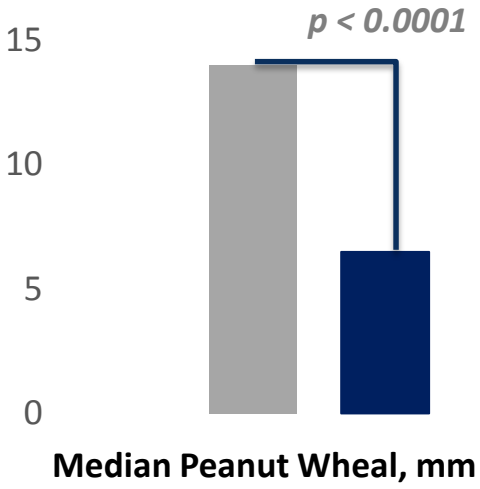
ARC002: Placebo Crossovers

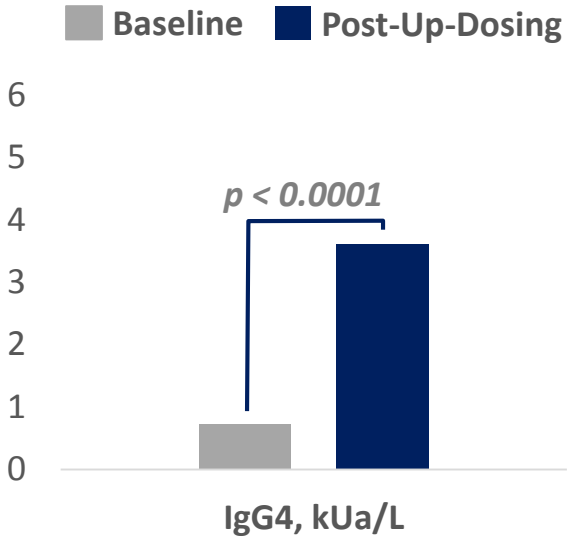


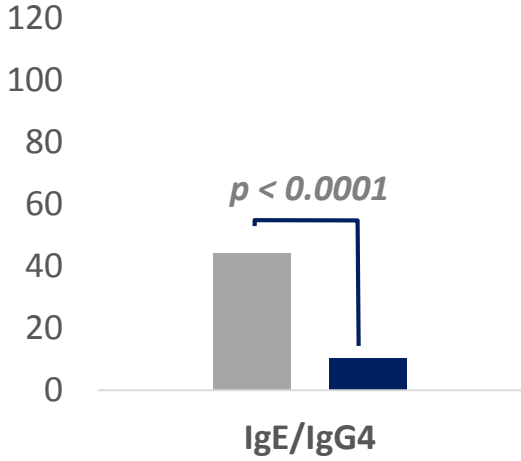




ARC001: Actives







Summary

- Placebo crossover, open label subjects confirmed findings from ARC001
  - Desensitization to 443 mg is achieved with ~22-week up-dosing period to 300 mg/d of AR101
- For those who completed approximately ~ 9 months of AR101 therapy (up-dosing and maintenance)
  - 100% tolerated 443 mg cumulative of peanut protein
  - 90% tolerated 1043 mg
  - 60% tolerated 2043 mg
- Preliminary evidence suggests that the safety and tolerability of AR101 improves during maintenance therapy relative to up-dosing

Conclusion and Next Steps

- AR101 appears to safely and effectively desensitize to peanut allergy in a controlled OIT regimen

- Next Steps
  - ARC002 Part II: Optional High-dose Up-Dosing and Extended Maintenance
    - Longer-term safety and tolerability
    - Longer-term changes in IgE and IgG4
  - PALISADE Phase 3 trial of AR101 (initiated 2015, enrolling)

Thank you for your attention

- Special thanks to 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
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  - Icahn School of Medicine at Mount Sinai - Sally Noone
  - University of North Carolina School of Medicine - Jill French and Pamela Steele

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