Efficacy and Safety of AR101 in Peanut Allergy: Results from a Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial (PALISADE)

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Disclosure

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- The committed research staff who conducted the study, collected, cleaned, analyzed and presented the data

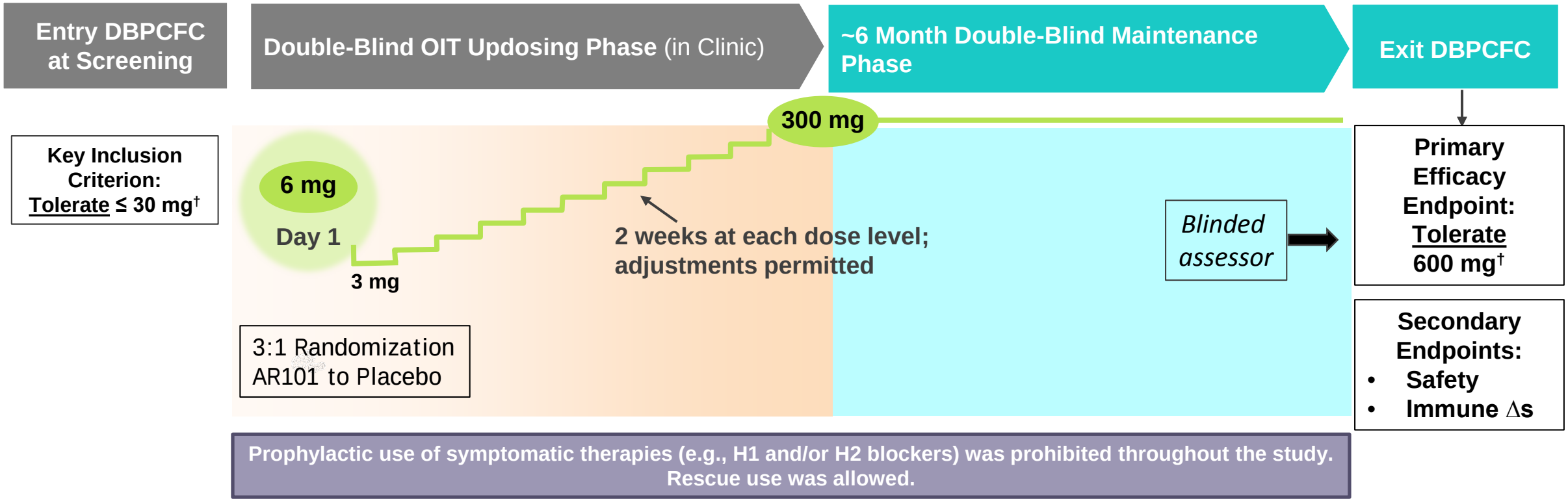
PALISADE
Peanut ALlergy Oral Immunotherapy Study of AR101 for DEsensitization

- International, multicenter, randomized, double-blind, placebo-controlled, Phase 3 study of AR101 in peanut-allergic individuals
- **Key Enrollment Criteria:**
  - Sensitization to peanut with clinical reactivity at ≤ 100 mg of peanut protein in a screening DBPCFC (i.e., tolerating no more than 30 mg at baseline)
  - Excluded for recurrent or chronic GI symptoms of any etiology, severe or poorly controlled asthma, or severe anaphylaxis occurring within 60 days of screening
- **Prespecified primary analysis:** children aged 4-17 years

AR101 is an investigational oral biologic drug product used for Characterized Oral Desensitization ImmunoTherapy (CODIT™) that contains the protein profile found in peanuts and is manufactured to current Good Manufacturing Practices (cGMP) specifications

Study Overview & Schematic

Participating countries (66 centers): US, Canada, Denmark, Germany, Ireland, Italy, Netherlands, Spain, Sweden, UK



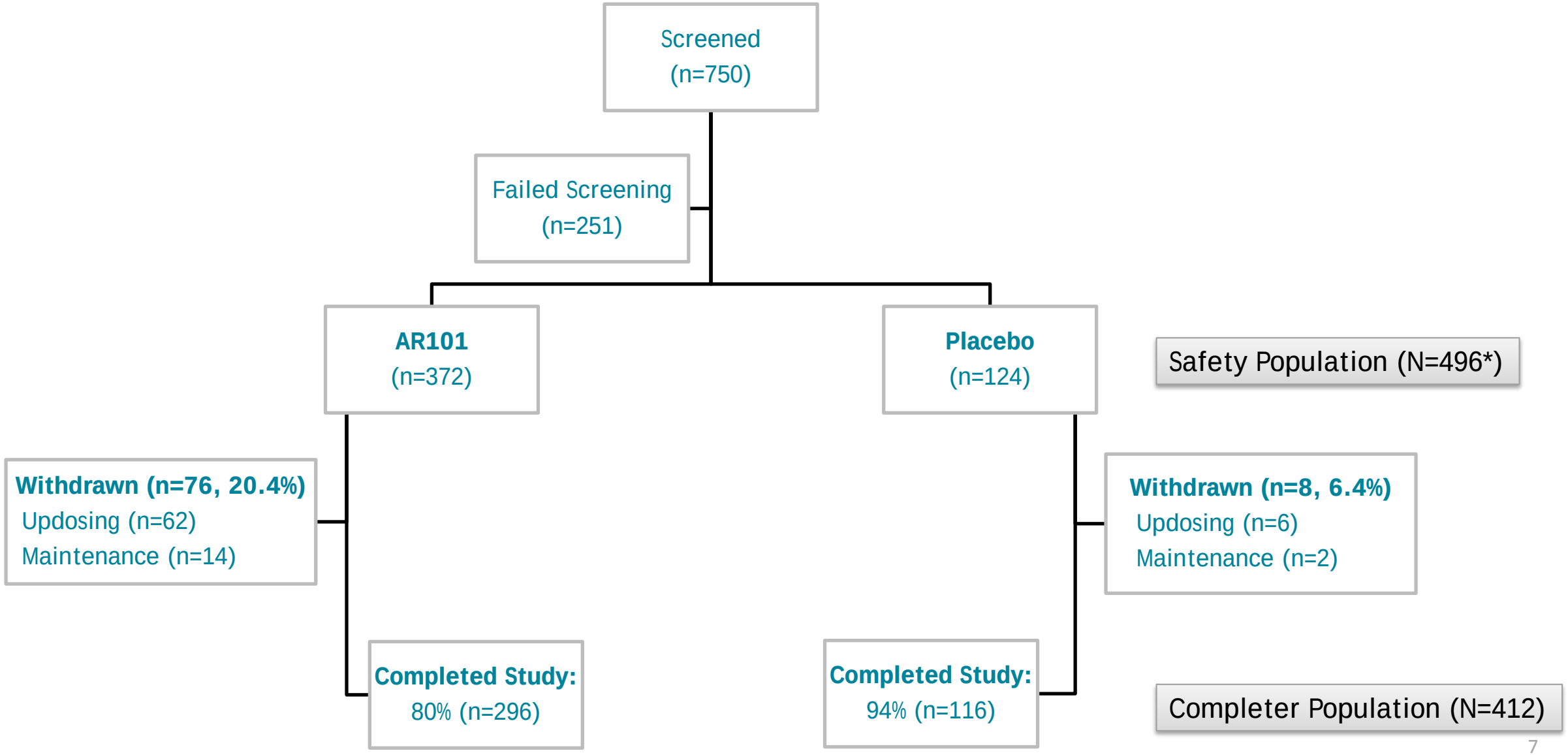
†600 mg of peanut protein is approximately equal to two peanut kernels

www.clinicaltrials.gov: NCT02635776

Baseline Characteristics: 4-17 year olds

Characteristic, n (%)	AR101 patients (n=372)	Placebo patients (n=124)	Totals (n=496)
Sex			
Male	208 (56%)	76 (61%)	284 (57%)
Age			
4-11 years	238 (64%)	89 (72%)	327 (66%)
12-17 years	134 (36%)	35 (28%)	169 (34%)
Race			
Non-Hispanic Caucasian	292 (78%)	97 (78%)	389 (78%)
Other	80 (22%)	27 (22%)	107 (22%)
Baseline peanut sensitivity			
Median (IQR) SPT average wheal (mm)	11 (9, 14.5)	12 (9, 15.3)	11 (9, 15)
Median (IQR) Peanut-specific IgE (kU_A/L)	69 (19, 194)	75 (29, 251)	71 (20, 202)
Median (IQR) maximum tolerated dose (mg)	10 (3,30)	10 (3,30)	10 (3,30)
History of pre-study peanut anaphylaxis	269 (72%)	89 (72%)	358 (72%)
Previous or present asthma	198 (53%)	65 (52%)	263 (53%)
Multiple food allergies	245 (66%)	80 (65%)	325 (66%)

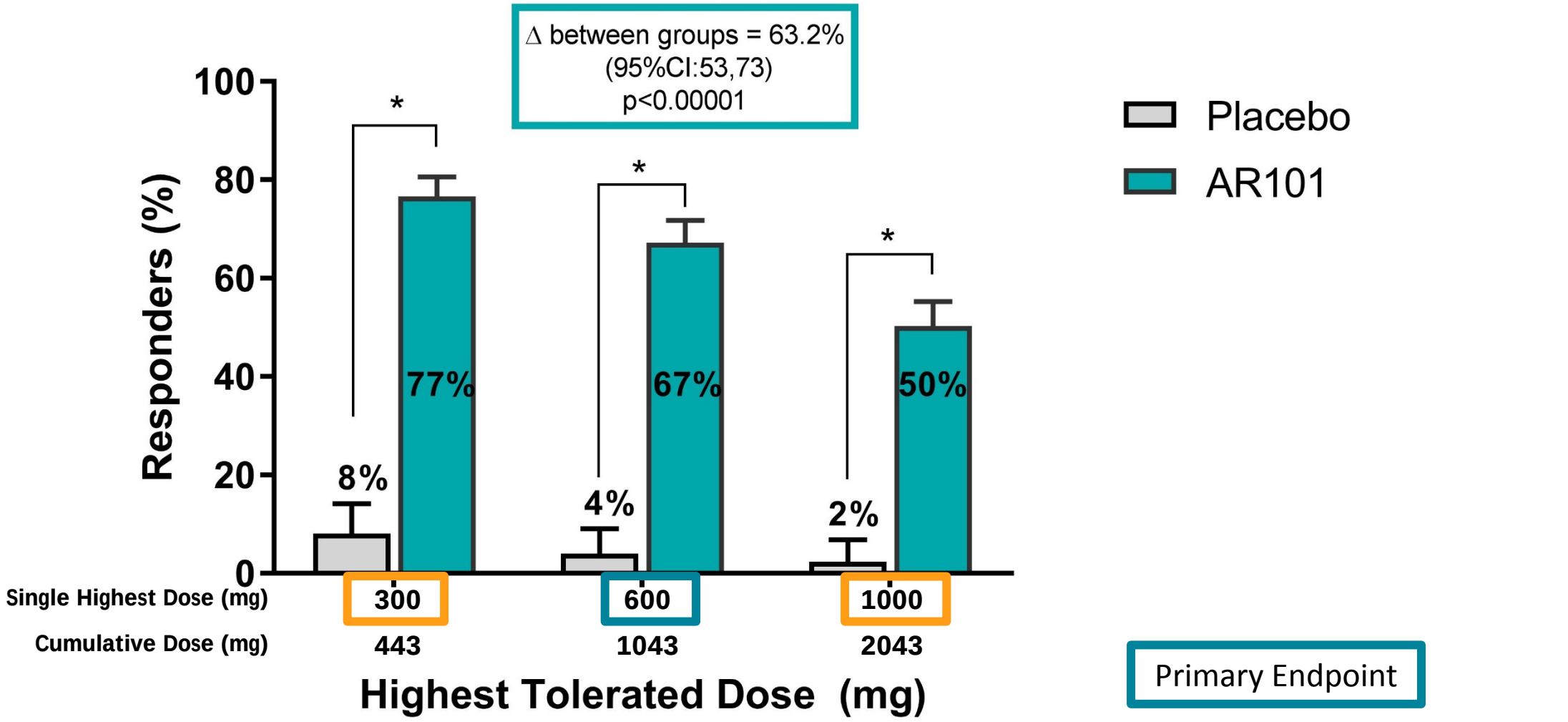
Participant Disposition: 4-17 year olds



*3 were randomized in error; 496 exposed to ≥ 1 dose of study product

Efficacy of AR101 in 4-17 year olds: ITT Population (N=496)

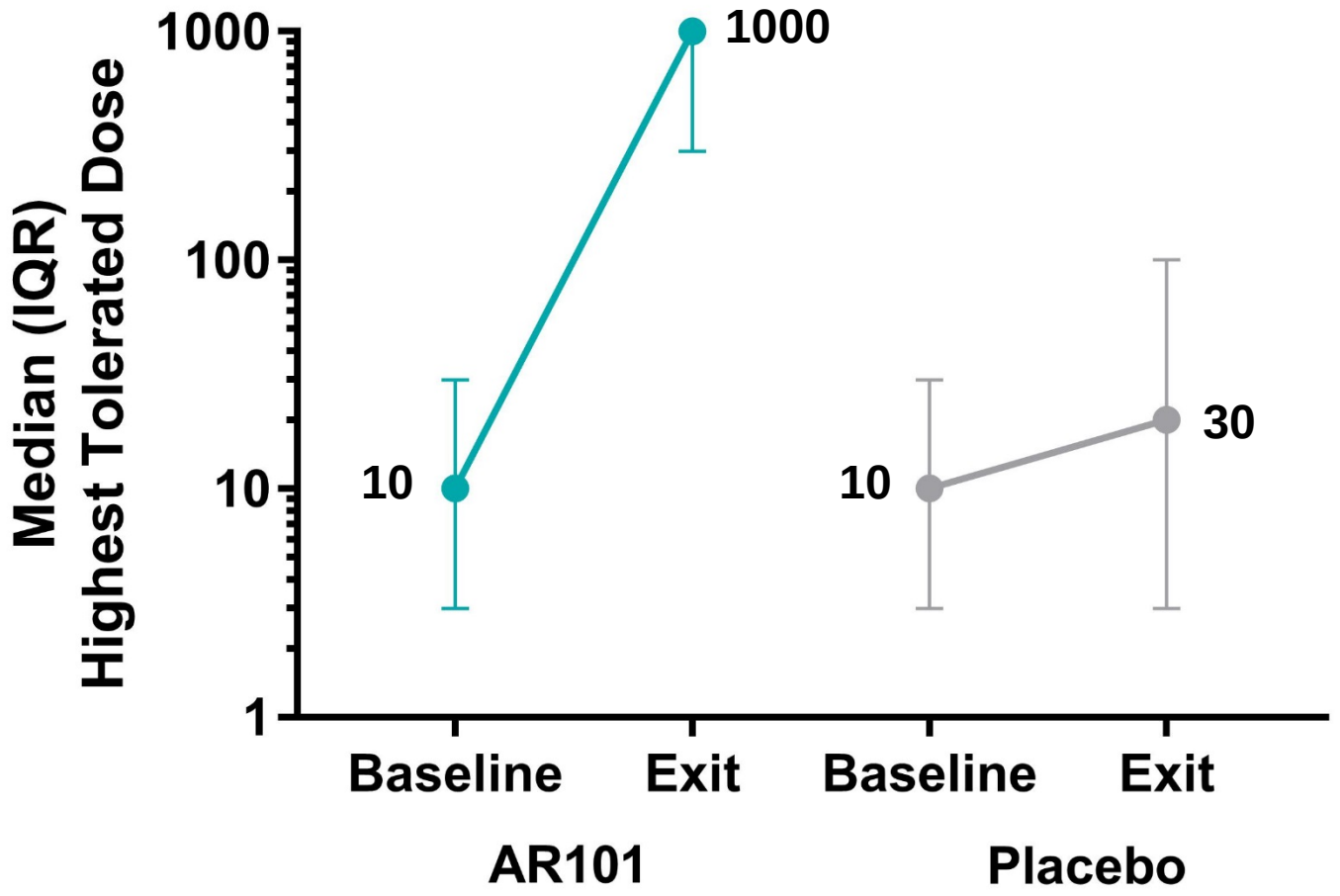
Assessed at Exit DBPCFC



*p<0.00001 for H_0:Treatment Difference = 15%

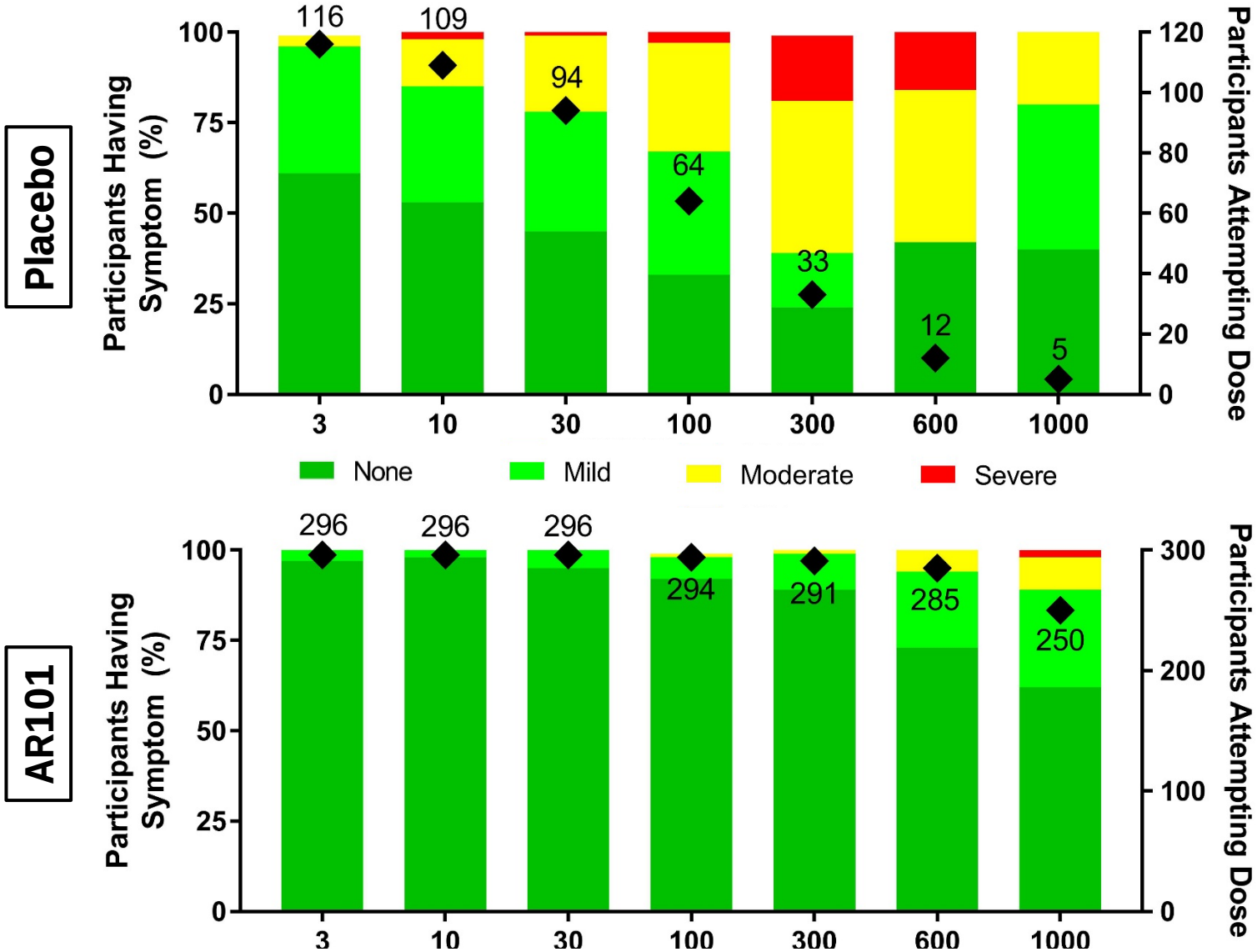
Highest Tolerated Single Challenge Dose: ITT Population

Median dose tolerated in Entry and Exit Peanut Challenges



Symptom Severity at Exit Peanut Challenge – Completers

DBPCFC Results as Evaluated by an Independent Blinded Assessor



Epinephrine Use†	AR101	Placebo
None	268 (91%)	54 (47%)
1	25 (8%)	43 (37%)
2	3 (1%)	17 (15%)
≥ 3	0	2 (2%)

†p<0.0001 for overall between-group difference

Key Findings

Compared to placebo, the AR101 group:

1. Developed fewer moderate and severe symptoms;
2. Required more peanut exposure to elicit the onset of symptoms;
3. Was more likely to complete the challenge; and
4. Needed less epinephrine.

Key Safety Events – Safety Population

- Approximately 99% of AR101-treated participants and 95% of placebo participants had a treatment-emergent (i.e., post-randomization) adverse event (AE)

- 9 SAEs in 8 AR101 participants (2.2%) and 1 SAE in 1 placebo participant (0.8%)
  - In the AR101-treated participants:
    - 5 events were unrelated to study drug; 4 were related
    - 5 events led to discontinuation
    - 1 event was severe and related - anaphylaxis early in maintenance; high baseline psIgE

- No deaths, life-threatening AEs, or suspected unexpected serious adverse reactions (SUSARs)

- 16 participants (4%) in the AR101 group discontinued the trial due to chronic/recurrent GI AEs
  - 1 AR101 participant was diagnosed with EoE and withdrew, with resolution of symptoms
  - 2 other participants had symptoms and negative EGDs

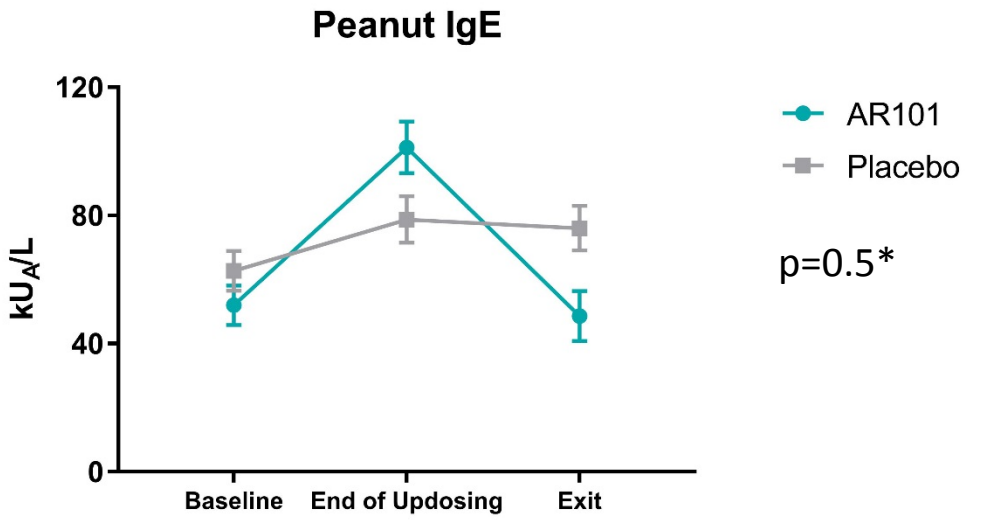
- 54 AR101 participants (14.5%) and 6 placebo participants (3.2%) had a treatment-emergent systemic hypersensitivity reaction
  - 98.2% of these events were graded mild or moderate
  - 10 AR101 participants (2.7%) discontinued as a result of these events

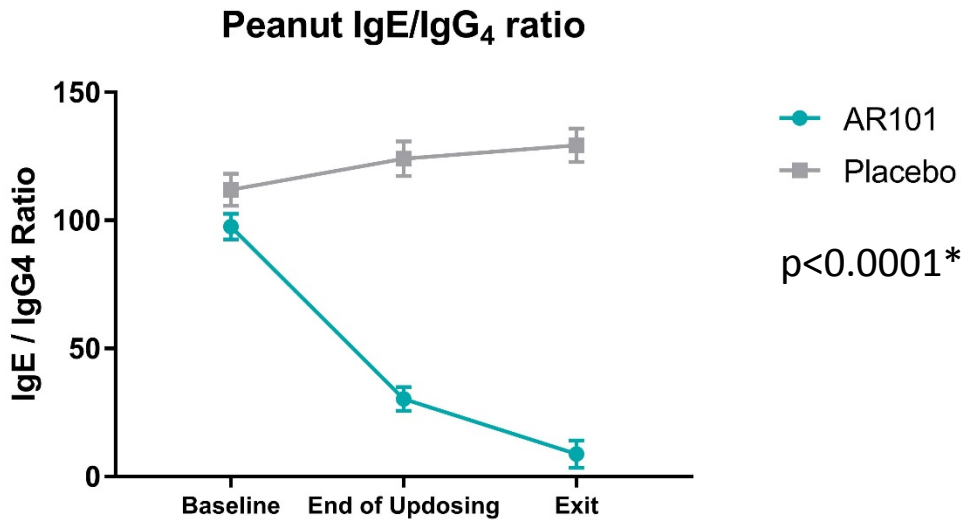
Study Discontinuations: 4-17 year olds

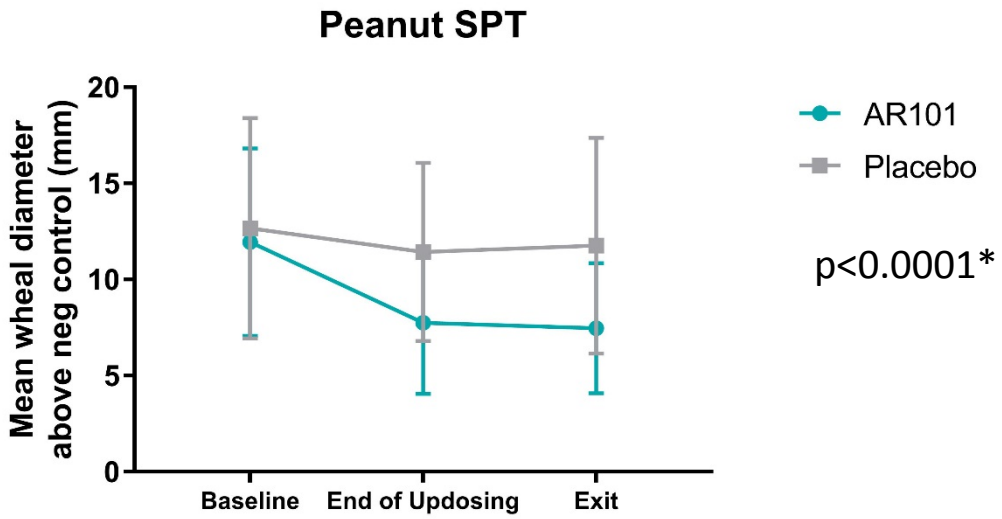
	AR101 (n=372)	Placebo (n=124)
Discontinuations	**N (%)**	**N (%)**
Withdrawals not due to AEs	30 (8.0)	6 (4.8)
Withdrawals due to AEs, total and by category	46 (12.4)	2 (1.6)
• Acute / Chronic / Recurrent GI[1]	25 (6.7)	0
• Systemic hypersensitivity reactions[2]	10 (2.7)	2 (1.6)[3]
• Respiratory system	4 (1.1)	0
• Cutaneous	3 (0.8)	0
• Other[4]	4 (1.1)	0

1: Includes one case of EoE; 2 additional participants had negative endoscopies and no additional cases of EoE were identified in the study
2: Of these, 7 were investigator-identified anaphylaxis events (1 severe)
3: 2 systemic reactions during up-dosing attributed to study product
4: Includes one discontinuation for each: acute viral illness, eye pruritus, headache, and an unknown factor

Immune Modulation by AR101







*p value refers to a between-group comparison of the change from Baseline to Exit using an ANCOVA model

Summary and Conclusions

- In this highly allergic population, 67% of AR101-treated participants successfully tolerated 600 mg of peanut protein at the exit food challenge, compared to 4% in placebo group
- The median tolerated dose improved 100-fold in AR101-treated participants from entry to exit food challenge; symptom severity and epinephrine use at exit were blunted
- SAEs, and withdrawals due to GI or hypersensitivity events affected <5%; no deaths or SUSARs
- Overall the safety profile of AR101 was similar to previous studies of oral immunotherapy
  - The frequency and severity of hypersensitivity AEs was as expected
  - The 6.7% rate of GI-related withdrawals, and one case of EoE, were lower than expected
- PALISADE was the largest peanut allergy trial ever conducted; the first to use an independent blinded assessor; and first to accept participants with severe or life-threatening history
- The data suggest that AR101 could potentially be useful in the treatment of peanut allergy in a highly sensitive population of children and adolescents