

FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Pulmonary-Allergy Drugs Advisory Committee (PADAC) Meeting
May 11, 2023

QUESTIONS

1. **DISCUSSION:** Discuss the pharmacokinetic/pharmacodynamic (PK/PD) approach for establishing efficacy for ARS-1 (epinephrine nasal spray) for the emergency treatment of allergic reactions (Type I) including anaphylaxis, specifically:
 - a. The PK-bracketing approach using approved epinephrine injection products.
 - b. The relevant PK/PD parameters to support clinical efficacy for the intended indication, including the significance of the following findings:
 - The diminished PK/PD sustainability in subjects with allergen-induced nasal congestion compared to epinephrine injection products and lack of data from repeat dosing under allergen-induced nasal congestion conditions.
 - The different PK comparisons of single-dose ARS-1 and Adrenalin in the first 10 minutes for Study EPI 15, EPI 16 (without allergen-induced nasal congestion), and EPI 17.
 - c. The uncertainty of translation of PK/PD results from healthy subjects and subjects with allergen-induced nasal congestion to patients with anaphylaxis, and whether clinical data are needed.
2. **VOTE:** Do the PK/PD results support a favorable benefit-risk assessment for ARS-1 in adults for the emergency treatment of allergic reactions (Type I) and anaphylaxis?
 - a. If not, what additional data are needed?
3. **VOTE:** Do the PK/PD results support a favorable benefit-risk assessment for ARS-1 in children (<18 years of age) ≥ 30 kg for the emergency treatment of allergic reactions (Type I) and anaphylaxis?
 - a. If not, what additional data are needed?