**Pharmacokinetics/Pharmacodynamics After Single and Repeat Administration of ARS-1 (neffy Nasal Spray), Epinephrine Auto-Injector, and Manual Intramuscular Injection**

### Rationale

- For immediate treatment for severe anaphylaxis and epinephrine autoinjectors or intramuscular epinephrine injection are widely prescribed. 1
- Despite drug similarity, pharmacokinetic results are variable due to differences in delivery methods and routes of administration.
- Nasal spray has the potential to deliver epinephrine directly to the systemic circulation by way of the nasal mucosa, which may lead to faster systemic availability and onset.
- Pharmacokinetic data are needed to better understand the potential for neffy nasal spray to deliver epinephrine.

### Methods

- The study was a first order, repeated, single-blind, randomised, crossover study conducted in 59 healthy subjects. The study was conducted on two separate occasions.
- Single and repeat dose treatment groups were administered, with each dose administered via intranasal and intramuscular routes.
- The study was conducted in two phases, with each phase separated by at least 14 days.
- At each treatment phase, one subject received neffy nasal spray, one received EpiPen 0.3 mg IM, and one received EpiPen 0.3 mg twice.
- Blood samples were collected at regular intervals for 360 minutes after the first dose.

### Results

#### Pharmacokinetic Results

- Following administration of neffy nasal spray, maximum plasma concentrations were highest after both EpiPen and neffy nasal spray, with neffy nasal spray resulting in a slight increase in systolic blood pressure (SBP) and diastolic blood pressure (DBP).
- Neffy nasal spray resulted in a slightly more rapid onset of pharmacodynamic effect compared to EpiPen, with the maximum pharmacodynamic effect occurring at 15 minutes after administration.
- Neffy nasal spray resulted in a higher maximum change in heart rate compared to EpiPen, with a maximum increase of 42 bpm observed with neffy nasal spray.

#### Pharmacodynamic Results

- Following administration of neffy nasal spray, there was a significant increase in SBP, DBP, and heart rate compared to baseline.
- Neffy nasal spray resulted in a more rapid and sustained increase in SBP compared to EpiPen, with a maximum increase of 42 mmHg observed with neffy nasal spray.
- Neffy nasal spray resulted in a more rapid and sustained increase in heart rate compared to EpiPen, with a maximum increase of 22 bpm observed with neffy nasal spray.

### Discussion

- Despite the similarities in drug composition, pharmacokinetic results indicate that neffy nasal spray may offer a faster and more sustained increase in SBP and heart rate compared to EpiPen.
- The faster and more sustained increase in SBP and heart rate observed with neffy nasal spray may provide a more robust cardiac response to the administration of epinephrine.
- Further studies are needed to evaluate the potential clinical benefits of neffy nasal spray compared to EpiPen.

### References