**Cardiovascular Profile of Dihydroergotamine Mesylate (DHE) Delivered by INP104 Compared to D.H.E. 45® for Injection From the INP104-101 Clinical Trial**

Karen Craig,1 John Hoekman,1 Maria Jeleva,1 Kelsey Satterly,1 Stephen Shrewsbury1

1Impel NeuroPharma

**Results**

### Introduction

- Dihydroergotamine (DHE), a synthetic derivative of ergotamine, has been utilized since 1930 to treat migraine and cluster headache.
- In the past, ergot alkaloids were the primary therapeutic agents for the treatment of migraine.
- However, ergot alkaloids exhibit a high rate of cardiotoxicity and vasospasm in higher doses.
- The Assembled INP014 Combination Product is a novel portable delivery system designed to deliver DHE in a stable aerosol form that is biocompatible and can be administered by patients with cardiovascular risk factors.
- Two studies have been performed: one of INP104-101 (2017) and one of INP104-102 (2018).
- INP104 (1.45 mg) delivered in one divided dose, i.e. one spray in each nostril, also delivered 0.88 mg of DHE.
- Migranal Nasal Spray delivered 7.9 mg of DHE.

### Trial Design

A Phase I, open-label, 3-way, 3-period cross-over study was conducted to determine the PK parameters and comparative CV profile.

### Blood Pressure Changes

- Analysis of change from baseline for the Safety population and PK population.
- Significantly lower diastolic BP was observed with INP104 compared to baseline measurements from 5 min to 30 min for both systolic and diastolic BP. The small increase in BP seen with INP104 was not statistically significant.
- INP104 was well tolerated and had fewer treatment-related adverse events in comparison to IV DHE.

### Pharmacokinetics

- No significant difference in the PK parameters and the comparative PK population.

### Conclusions

- DHE was well tolerated and provided effective treatment for migraine.
- No significant changes in heart rate or systolic BP were observed.
- The cardiac adverse events associated with IV DHE were not observed with INP104 administration.

### Advantages Related to IV DHE Not Observed With IV DHE

- Reduced treatment-related adverse events.
- Improved patient comfort and compliance.
- Enhanced patient safety.

### References