Nasal Safety of Chronic Intermittent Use of INP104: Results From the Phase 3 Open-label STOP 301 Study

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Introduction

• INP104 is an investigational, drug-device product that delivers doxycycline directly to the upper nasal space via Precision Olfactory Delivery (POD) technology (for the diagnosis, treatment, and/or management of rhinosinusitis).

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• Primary endpoints were the number of patients with serious and non-serious treatment-emergent adverse events (TEAEs), change in nasal mucosal integrity observed on endoscopy, and change in function of the nose.

• Serial endoscopy of patients with rhinosinusitis is standard of care.

• Since a standardized objective safety assessment instrument for the upper nasal space was not previously available, Impel NeuroPharma worked closely with experts in the field to design appropriate scales to assess changes to the upper nasal space in the STOP 301 study.

Methods

• **Study Design**
  - STOP 301 was a Phase 3, open-label, single-arm assignment study (NCT02015731).

  - 6-week screening period, in which patients used their first nasal care to treat rhinitis attacks (MA), a 24-week treatment period for all patients, a treatment extension to 52 weeks for a subset of the patients, and a 2-week post-treatment follow-up period.

  - Following the screening period, all patients were provided with up to 3 times/ week of INP104 to self-administer (0.4 mg inh via a 21 gauge needle) with self-reported MA.

• **Study Patients**
  - Age ≥ 18 years old
  - History of CRS with nasal polyps (NPS) per 2015 ISAC criteria and/or 2019 European Society of Otolaryngology–Head and Neck Surgery criteria
  - Disease severity of moderate to severe nasal polyps as a consequence of CRS
  - Nasal obstruction and rhinorrhea
  - Adults with nasal obstruction, with a minimum of 2 MAs, with or without mucous, each month without dramatically improving in at least 3 of 4 (MA days/month).

• **Study Outcomes**
  - Nasal Safety Review Committee (NSRC) consisting of 3 independent otorhinolaryngologists, participated in the development and evaluation of safety monitoring tools.

  - **Upper endoscopy**
    - 40-item clinical and stratified test performed approximately every 12 weeks.
    - A significant change in the UPSS score was defined as a ≥5-point reduction based on the best current evidence.

  - **Nasal Endoscopy**
    - Nasal TEAE monitoring revealed that a small percentage of patients experienced nasal events (4% to 9.5% of patients at each visit).

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Objectives

• To assess the safety and tolerability of long-term intermittent use of INP104 on the nasal mucosa and effects for 24 and 52 weeks in the STOP 301 study.

• Nasal Endoscopy changes (Figure 1)
  - Performed by an otorhinolaryngologist using a NO-NM to measure mucosal integrity and mucosal status, systemic, respiratory, and nasal mucosa.

  - Performing the nasal endoscopy before the first visit and by baseline and at 6, 12, 18, and 24 weeks, and 36 and 52 weeks for extension.

  - A total score ≥ 7 (right upper nasal space), or an individual score ≥ 2 on any item at any time point triggered a repeat examination 2 weeks later.

  - Nasal AEs, defined as AEs associated with the nose in any way, were identified using a custom Medical Dictionary for Regulatory Activities (MedDRA) query list.

  - Minimal mean decreases (<0.5) and mean increases/decreases (≥0.5) from baseline were recorded as the TEAE.

• **Quantitative Scoring Scale for Evaluation of the Nasal Mucosa (QSS-NM)**
  - Up to 3 times/week of INP104 to self-administer (0.4 mg inh via a 21 gauge needle) with self-reported MA.

• **Nasal TEAEs**
  - Nasal TEAEs were identified during the previous 6 months during the follow-up period.

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• **Nasal Endoscopy Findings**
  - Nasal endoscopy findings were reviewed and captured in a customized database.

  - Nasal AEs were identified during the previous 6 months.

• **Nasal TEAEs Associated With Nasal Endoscopy and UPSIT Findings**
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