Development of a Precision Olfactory Delivery (POD®)-Olanzapine Drug-Device Product for Agitation.

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Abstract

Background: Impel NeuroPharma is developing INP105 (POD®-Olanzapine [OLZ]), a drug-device combination product consisting of a novel OLZ powder formulation for nasal administration by the POD device, designed to provide a dose form with rapid onset of agitation relief comparable to intramuscular injections and the ease of use of oral therapy. POD OLZ is designed to deliver 2 mg olanzapine, the systemic dose for rapid and consistent absorption with minimal effort or user coordination.

Methods: OLZ formulations were designed and manufactured for nasal upper respiratory delivery. Formulations were characterized by analytical methods and in vitro and non-human primate (NHP) pharmacokinetic (PK) studies. OLZ formulations were delivered nasally to NHP by Impel’s non-human primate (NHP) pharmacokinetic (PK) studies.

Results: Approximately 30 formulations were designed for nasal delivery. The POD device, manufactured, and analyzed by analytical methods and device compatibility. The lead formulation was tested in 5 months of stability, ~98% loss and 1% increase over the shelf-life period, and exhibited T_{max} = 17 minutes, similar to control, and a C_{max} of 71 ng/mL, ~3-fold higher than the C_{max} following intramuscular OLZ in patients.

Conclusions: This series of preclinical development studies demonstrates:

- Impel NeuroPharma is developing INP105, a POD®-OLZ drug-device combination product, which will administer OLZ through nasal powder formulations delivered to the upper nasal mucosa for rapid and consistent systemic absorption with minimal effort or user coordination.

Introduction

Acute agitation is a behavior observed in multiple psychiatric diseases, with in 7 million episodes reported per year in the US, and which can improve the likelihood of violent behavior. Bipolar psychoses, including OLZ and olanzapine, have been approved for chronic and acute agitation treatment, respectively, for schizophrenia and bipolar disorder in the US for over 2 decades. During acute agitation episodes, the POD device can be administered as rescue medication due to its user-friendly design and rapid administration, which can be beneficial in the management of acute agitation. Emergency Room (ER) or other acute hospital settings and may require restraint if the patient is agitated. Agitation treatment is often challenging due to uncontrollable factors, such as the high likelihood of injuries. When possible, non-injectable routes of administration are preferred during uncooperative, potentially reducing trust between patient and medical personnel and increasing the likelihood of injuries. When possible, non-injectable routes of administration are preferred during uncooperative, potentially reducing trust between patient and medical personnel and increasing the likelihood of injuries.

Methods

Manufacturing and Analytical Testing

- OLZ formulations were designed and manufactured for nasal upper respiratory delivery.
- Key characteristics were optimized for POD device compatibility.
- Formulations were identified by analytical methods and in vitro and non-human primate (NHP) pharmacokinetic (PK) studies.

Results

Approximately 30 formulations were designed for nasal delivery by the POD device, manufactured, and analyzed by analytical methods and device compatibility. The lead formulation was tested in 5 months of stability, ~98% loss and 1% increase over the shelf-life period, and exhibited T_{max} = 17 minutes, similar to control, and a C_{max} of 71 ng/mL, ~3-fold higher than the C_{max} following intramuscular OLZ in patients.

Conclusions

- Impel NeuroPharma is developing INP105, a POD®-OLZ drug-device combination product, which will administer OLZ through nasal powder formulations delivered to the upper nasal mucosa for rapid and consistent systemic absorption with minimal effort or user coordination.
- This series of preclinical development studies demonstrates:
  - Impel NeuroPharma is developing INP105, a POD®-OLZ drug-device combination product, which will administer OLZ through nasal powder formulations delivered to the upper nasal mucosa for rapid and consistent systemic absorption with minimal effort or user coordination.
  - The POD device, a needle-free, easy self- or care-giver administered, and potentially rapidly effective OLZ treatment for short episodes of acute agitation in the behavioral communities in ER settings.
  - The POD device can be administered as rescue medication due to its user-friendly design and rapid administration, which can be beneficial in the management of acute agitation. Emergency Room (ER) or other acute hospital settings and may require restraint if the patient is agitated. Agitation treatment is often challenging due to uncontrollable factors, such as the high likelihood of injuries. When possible, non-injectable routes of administration are preferred during uncooperative, potentially reducing trust between patient and medical personnel and increasing the likelihood of injuries.

References

Impel NeuroPharma, a leader in the field of precision drug-delivery device development in the INP105-101 Clinical Study.

Figure 1a. Image of the Clinical Research INP15 (POD®-OLZ) Drug-Device Combination Product Utilized in the INP105-101 Clinical Study

Figure 1b. Diagram of the Nasal Space: "Lower" Is the Target of Typical Oral Olanzapine Formulations.

"Upper" Is the Target of the POD-OLZ Device

Figure 2. Image of the INP-POD Device

Figure 3. Mean (± SD) Plasma Concentrations of OLZ Following Administration of Nasal Powder Formulations Delivered to NHP by the POD Device (Time displayed 0-2 hours)

Figure 4. Mean (± SD) Plasma Concentrations of OLZ Following Administration of Nasal Powder Formulations Delivered to NHP by the POD Device (Time displayed 0-10 hours)

Table 1. Summary of Select Formulation Stability Results under Accelerated (40 °C/75% RH) Storage Conditions

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Stability Results</th>
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<tbody>
<tr>
<td>F-OLZ #1</td>
<td>A</td>
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<tr>
<td>F-OLZ #2</td>
<td>A</td>
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<tr>
<td>F-OLZ #3</td>
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<td>F-OLZ #4</td>
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<td>F-OLZ #5</td>
<td>A</td>
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<tr>
<td>F-OLZ #6</td>
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</tbody>
</table>

Conclusions

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- The POD device, a needle-free, easy self- or care-giver administered, and potentially rapidly effective OLZ treatment for short episodes of acute agitation in the behavioral communities in ER settings.
- This series of preclinical development studies demonstrates:
  - The POD device can be administered as rescue medication due to its user-friendly design and rapid administration, which can be beneficial in the management of acute agitation. Emergency Room (ER) or other acute hospital settings and may require restraint if the patient is agitated. Agitation treatment is often challenging due to uncontrollable factors, such as the high likelihood of injuries. When possible, non-injectable routes of administration are preferred during uncooperative, potentially reducing trust between patient and medical personnel and increasing the likelihood of injuries.
  - The results from these development studies has led to the identification of a lead formulation to be tested in an INP105-101 pivotal clinical study for further development.

References