Pharmacokinetic Evaluation of Subcutaneously Administered ZYN001 in Male Sprague-Dawley Rats

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Objectives

The objective of this study was to evaluate the in vivo pharmacokinetics of ZYN001 — specifically to confirm in vivo with respect to general health and any signs of disease during the acclimation period, animals were observed daily with respect to general health and any signs of disease. In some patients, these side effects may limit the therapeutic use of THC.

Methods

A total of 3 male experimentally naïve Sprague-Dawley rats were included in this study. During the acclimation period, animals were observed daily with respect to general health and any signs of disease. In some patients, these side effects may limit the therapeutic use of THC.

Results

Methods cont.

• ZYN001 rapidly converted to THC within 0.08 hours (54.8 minutes)
• THC plasma concentration ranged from 159.6 at 0.08 hours postdose to 93.3 ng/mL, at 74.75 hours postdose
• Plasma concentrations of ZYN001 ranged from 26.4 ng/mL at 0.08 hours postdose to 17.4 ng/mL at 74.75 hours postdose
• Concentration of metabolites were consistent and low (<5 ng/mL) at each time point postdose

Conclusions

• Rat subcutaneous dosing proved to be an excellent tool for observing chemical characteristics of a THC produrg delivered just beneath the skin’s surface
• ZYN001 was rapidly hydrolyzed to THC within 5 minutes of subcutaneous dosing
• Low levels of THC’s main metabolites, THC-OH and THC-COOH, were observed over the course of the study period
• Since THC-OH is a potent psychoactive metabolite that crosses the blood-brain barrier more easily than THC, low levels in plasma may reduce the likelihood that patients will experience treatment-emergent psychotropic effects in patients
• Based on the results of this study, ZYN001, given in the form of a transdermal delivery system, should rapidly hydrolyze to THC, bypass first pass metabolism to THC’s main metabolites and thereby reduce treatment-emergent psychotropic effects in patients

References


Table 1. Plasma concentrations of ZYN001 in Sprague-Dawley rats (n = 3)

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<th>0.08</th>
<th>0.25</th>
<th>1</th>
<th>3</th>
<th>6.67</th>
<th>24.11</th>
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<td>27.2</td>
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<td>THC</td>
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<td>135.4</td>
<td>107.7</td>
<td>153.2</td>
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<td>3.1</td>
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Figure 1. Hydrolysis of ZYN001 into glyceric acid and THC

Figure 2. Plasma concentration vs time in rats after 1 mg/kg subcutaneous administration of ZYN001

Photo Credit: Zynexa Pharmaceuticals Inc.