Development of a novel Drug Delivery System 2 (DDS2) for colon targeted delivery treatment of ulcerative colitis

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Autonomous Capsule Localization

The autonomous localization technology was developed with a comparable prototype, the Telemetric Localization Capsule (TLC), in 58 subjects across three clinical studies to validate and improve the technology and internal algorithm used for localization. The localization system identifies different anatomical regions by emitting colored light that interacts with the local GI environment and returns to spatially separated detectors. Measured light levels are analyzed by the algorithm to detect changes associated with different anatomical features. Upon detection of entry into the colon (S4), the DDS2 capsule initiates the gas cell actuator for drug release.

The DDS2 Capsule

The DDS2 is comprised of a drug reservoir that houses a liquid formulation of the therapeutic compound, a removable cap, and an electronic module (Figure 1). The electronic module houses the localization system, optical detection, and the gas cell required for releasing the drug formulation in the target location (Figure 1A).

Methodology

This study was conducted to demonstrate the functionality of the DDS2 after oral administration (PO) in fasted male beagle dogs pre-treated with pentagastrin (6 μg/kg IV to IV 9-14 h). The DDS2 drug reservoir was loaded with two marker drugs, acetaminophen (30.4 mg) and sulfasalazine (21.3 mg), the afternoon before administration and stored at room temperature. Blood sampling occurred at the following time points: Pre-dose, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 7.0, 8.0, and 24 hours post-dose to generate plasma concentration curves for both marker drugs (Figure 3).

Fecal samples were carefully monitored up to 72 hours post-dose to recover DDS capsules. The localization data were then extracted from the recovered capsule and analyzed.

Figure 2. Proprietary localization technology enables precision medicine for targeted therapeutics. The internal algorithm can detect five major anatomical locations to trigger various functions: (1) stomach, (2) pylorus, (3) small intestine, (4) colon, and (5) rectum.

Figure 1. Drug Delivery System 2 (DDS2) in an anatomical environment. 1: Photograph of Drug Delivery System 2 (DDS2); 2: Rendering of planned commercial DDS2.

Results

All capsules indicated the S4 trigger (entry into the colon) required for the gas cell actuator to start and stop. The reported event times are indicated in Table 1.

Gas cell start times in S5 capsules coincided with the associated S4 trigger times and ended 30 minutes post-starting time.

Comparison of the pharmacokinetic profile of acetaminophen and sulfapyridine indicated drug release in the colon shortly after self-determined delivery trigger (S4) around 4.5 hours post-dose in 4/5 capsules (Figure 3).

In the one remaining capsule, the drug release was after the first 8-hour post-dose blood sampling schedule but was later detected at the 24-hour timepoint and confirmed that the capsule functioned as intended.

Table 1. Localization and actuator events recorded on DDS2 capsules. The event log was examined to determine the localization event times of gas cell actuator start and stop.

<table>
<thead>
<tr>
<th>Animal #</th>
<th>Capsule #</th>
<th>S4 (min)</th>
<th>Gas Start (min)</th>
<th>Gas End (min)</th>
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<td>278.00</td>
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</tbody>
</table>

Summary and Conclusions

The pre-clinical study demonstrated that the Drug Delivery System 2 (DDS2) successfully autonomously identified the colon entry (S4) and delivered the marker drugs to the colon.

The DDS2 enables more precise dosing and higher local concentrations at the site of inflammation to increase tissue concentration, reduce systemic exposure, and address the need for more efficient colonic delivery of therapeutics for improved safety.

By leveraging a compound with proven efficacy, such as adalimumab or tofacitinib, in a soluble formulation, the DDS2 has the potential to apply this novel platform technology to address the unmet need of mucosal targeted therapy for inflammatory bowel disease.

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Reference


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