



*These Clinical Study Results are provided for informational purposes only.*

The study listed may include approved and non-approved uses, formulations or treatment regimens. It is not intended to promote any product or indication and is not intended to replace the advice of a health care professional. The results reported in any single clinical trial may not reflect the overall results obtained across the product development. Only a physician can determine if a specific product is the appropriate treatment for a particular patient. If you have questions, please consult a health care professional. Before prescribing any product, healthcare professionals should consult prescribing information for the product approved in their country.

## 2. STUDY SYNOPSIS

<b>Name of Sponsor/Company:</b> Biogen Idec Inc.	<b>Individual Study Table Referring to Part &lt;&gt; of the Dossier</b>  <b>Volume:</b>  <b>Page:</b>	<i>(For National Authority Use only)</i>
<b>Name of Finished Product:</b> Tonapofylline (BG9928)	<b>Name of Active Ingredient:</b> Tonapofylline (BG9928)	<b>Study Indication:</b> Hepatic Impairment
<b>Title of Study:</b> An Open-Label, Single-Dose Study to Assess the Pharmacokinetics, Safety, and Tolerability of Oral BG9928 in Subjects with Mild and Moderate Hepatic Impairment and in Healthy Subjects		
<b>Study Period:</b> Date of first treatment: 22 April 2009 End of Study Date: 07 July 2009	<b>Phase of Development:</b> 1	
<b>Study Objectives:</b> Primary Objective: <ul style="list-style-type: none"> <li>• to evaluate the effect of hepatic function on the pharmacokinetics of a single oral dose of tonapofylline in subjects with mild and moderate hepatic impairment and in subjects with normal hepatic function.</li> </ul> Secondary Objectives: <ul style="list-style-type: none"> <li>• to assess the effect of hepatic function on the safety and tolerability of single oral doses of tonapofylline in subjects with mild and moderate hepatic impairment and in subjects with normal hepatic function.</li> <li>• to assess the pharmacodynamics of single oral doses of tonapofylline in subjects with mild and moderate hepatic impairment and in subjects with normal hepatic function.</li> </ul>		

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<p><b>Study Design:</b></p> <p>This was to be an open-label, single-dose study in subjects with mild and moderate hepatic impairment and in subjects with normal hepatic function. Up to 28 subjects at 2 sites were to receive a single oral 75 mg dose of tonapofylline. Subjects were to be followed in the clinic for serial collection of blood, urine specimens, and clinical assessments for 96 hours postdose. Subjects were to be contacted by telephone on Day 7 to monitor and record concomitant therapy and adverse events (AEs).</p> <p>The study period was to consist of Screening, an inpatient predose period, an inpatient treatment period, an inpatient post-treatment period, and a telephone follow-up. Subject eligibility for the study was to be determined within 28 days prior to dosing.</p> <p>Each subject in the mild hepatic impairment group (Group 1) and moderate hepatic impairment group (Group 2) were to be matched with a healthy volunteer (Group 3) with regard to age (<math>\pm 5</math> years) and weight (<math>\pm 10\%</math>). There was to be at least 2 subjects of each sex in each group. Six subjects were to be enrolled in Group 1, and 8 subjects were to be enrolled in Group 2. Between 8 and 14 healthy volunteers were to be enrolled in Group 3 since 1 healthy volunteer could match 1 subject from each of the 2 hepatic impairment groups.</p> <p>Although the study was completed, Biogen Idec has decided not to pursue development of tonapofylline. Therefore, pharmacokinetic and pharmacodynamic parameters were not calculated and only safety results are presented.</p>		
<p><b>Number of Subjects (Planned and Analyzed):</b></p> <p>Up to 28 subjects were planned and 23 subjects were analyzed.</p>		

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<p><b>Study Population:</b></p> <p>Key Inclusion Criteria:</p> <ul style="list-style-type: none"> <li>• Must have been between the ages of 18 and 75, inclusive.</li> <li>• Must have had a body mass index between 19 kg/m<sup>2</sup> and 36 kg/m<sup>2</sup>, inclusive.</li> </ul> <p>The following criteria applied only to subjects enrolled into Groups 1 and 2 (mild or moderate hepatic impairment):</p> <ul style="list-style-type: none"> <li>• Must have had stable hepatic disease (i.e., no change in disease status within the last 2 months as determined by the enrolling Investigator) with laboratory and clinical findings that support the diagnosis of hepatic impairment.</li> <li>• Must have had a total Child-Pugh score of 5 to 6 (mild) or 7 to 9 (moderate).</li> <li>• Must have been otherwise healthy as determined by the Investigator on the basis of pre-study physical examination, medical history, 12-lead electrocardiogram (ECG), vital signs, and clinical laboratory parameters. Subjects with controlled hypertension and those problems directly associated with the primary diagnosis of hepatic impairment may have been included. Subjects with stable, mild, chronic concurrent diseases, such as degenerative joint disease, may have been included.</li> </ul> <p>Key Exclusion Criteria:</p> <ul style="list-style-type: none"> <li>• History of an allergic reaction to any methylxanthine-containing compound.</li> <li>• History of seizure within the past 10 years, or use of any medication for the suppression of seizures within the past 5 years.</li> <li>• History of brain surgery, meningitis/encephalitis, penetrating head trauma, stroke, or transient ischemic attack within the past 6 months.</li> <li>• History of active (within 6 months) drug or alcohol abuse, a positive drug screen (without a medically indicated rationale), or a positive alcohol breath test at Screening or on Day -2.</li> <li>• History of human immunodeficiency virus antibody.</li> <li>• Serious systemic infection (e.g., septicemia) within the 30 days prior to Day 1.</li> <li>• Fever, with body temperature &gt;38°C, within the 48 hours prior to Day 1.</li> <li>• Active bacterial or viral infection.</li> </ul>		
<p><b>Study Treatment, Dose, Mode of Administration, Batch Number:</b></p> <p>Subjects received a single oral 75 mg dose of tonapofylline. Batch number: <span style="background-color: black; color: black;">XXXXXXXXXX</span></p>		

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<b>Duration of Treatment and Follow-Up:</b> <u>Treatment period:</u> Subjects were to receive a single oral dose of tonapofylline and remain in the clinic (Day 1).  <u>Follow-up period:</u> Subjects were to remain in the clinic for 96 hours after dosing (Days 1 through 4). Subjects were to be contacted by telephone on Day 7.		
<b>Criteria for Evaluation:</b> <u>Safety:</u> <ul style="list-style-type: none"> <li>• AEs</li> <li>• serious adverse events (SAEs)</li> <li>• reasons for discontinuation of study treatment or the study</li> <li>• laboratory abnormalities</li> <li>• electrocardiogram (ECG) abnormality results</li> <li>• abnormalities observed from vital signs</li> <li>• abnormalities observed from physical examinations</li> </ul>		

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<p><b>Results:</b></p> <p><u>Subject disposition:</u></p> <p>Twenty-four subjects were enrolled at 2 study sites in the United States. One subject withdrew from the study before dosing due to a fever. Of the 23 subjects dosed, 9 subjects had normal hepatic function, 6 subjects had mildly impaired hepatic function, and 8 subjects had moderately impaired hepatic function. All 23 subjects completed treatment and the study.</p> <p><u>Demographics and smoking history:</u></p> <ul style="list-style-type: none"> <li>• Most subjects were white (96%), male (61%), and ranged in age from 44 to 66 years of age.</li> <li>• Eleven of the 23 subjects had a history of smoking and 8 subjects were current smokers.</li> </ul> <p><u>Safety:</u></p> <ul style="list-style-type: none"> <li>• Six of the 23 subjects dosed experienced a treatment-emergent AE: 3 subjects with mildly impaired hepatic function and 3 subjects with moderately impaired hepatic function.</li> <li>• Five subjects experienced a related AE.</li> <li>• One subject in the moderately impaired hepatic function group experienced a moderate AE (hematoma); all other subjects experienced mild AEs.</li> <li>• No severe AEs or SAEs, deaths, or discontinuations due to an AE occurred during the study.</li> <li>• No subject had any clinically significant changes from baseline in hematology, blood chemistry, vital sign measurements, physical examination findings, or ECG results.</li> </ul>		
<p><b>Conclusions:</b></p> <ul style="list-style-type: none"> <li>• A single oral dose of 75 mg of tonapofylline was well tolerated in these subjects.</li> <li>• There were no unexpected safety findings in this study.</li> </ul>		
<p><b>Publication(s) Based on the Study:</b></p> <p>None.</p>		
<p><b>Date of Report:</b> 10 May 2010</p>		