**Interim Analysis Report**

**Study Title:**  
A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study to Evaluate the Safety and Efficacy of Novostatin (Novitor) in Patients with Hypercholesterolemia

**Protocol Number:** NSP-002-2024  
**Study Duration:** March 2, 2024 – September 22, 2024  
**Sponsor:** Novitor Pharmaceuticals Inc.  
**Interim Analysis Date:** July 15, 2024  
**Data Cut-Off Date:** July 10, 2024

**1. Introduction**

This Interim Analysis Report summarizes the safety and efficacy data collected up to July 10, 2024, from the ongoing Phase 2 trial of Novostatin (Novitor). The interim assessment was conducted to evaluate the overall performance of the study, review emerging trends, and confirm the appropriateness of continuing the trial with the current protocol. The data are also intended to support the decision to progress to Phase 3 trials.

**2. Objectives of Interim Analysis**

**2.1 Primary Objectives**

* **Efficacy:**  
  Evaluate the mean percentage change in LDL cholesterol from baseline to Week 12 among subjects treated with Novostatin compared to placebo.

**2.2 Secondary Objectives**

* **Safety:**  
  Assess the incidence and severity of adverse events (AEs) and serious adverse events (SAEs) up to the interim cut-off.
* **Pharmacokinetics (PK):**  
  Review preliminary PK parameters in a subset of subjects.
* **Exploratory Endpoints:**  
  Monitor changes in total cholesterol, HDL, and triglycerides; and review early biomarker data.

**3. Interim Analysis Methodology**

**3.1 Analysis Population**

* **Intent-to-Treat (ITT) Population:**  
  All randomized subjects who have received at least one dose of study medication and have at least one post-baseline LDL measurement.
* **Safety Population:**  
  All subjects who received at least one dose of study medication.
* **PK Subset:**  
  Subjects with sufficient concentration-time data to evaluate PK parameters.

**3.2 Statistical Methods**

* **Primary Efficacy Analysis:**  
  An analysis of covariance (ANCOVA) model was used with the percentage change in LDL cholesterol as the dependent variable, adjusting for baseline LDL levels and treatment group.
* **Safety Analysis:**  
  A descriptive summary of AEs, SAEs, and laboratory abnormalities.
* **Interim Data Review:**  
  Data were summarized using descriptive statistics, and Kaplan–Meier estimates were generated for time-to-event analyses where applicable.

**4. Interim Analysis Results**

**4.1 Enrollment and Demographics**

* **Total Subjects Randomized (Interim):** 150
* **Novostatin Arm:** 75 subjects
* **Placebo Arm:** 75 subjects
* **Mean Age:** 56 years (range: 45–70)
* **Gender Distribution:** 52% Male, 48% Female

**4.2 Efficacy Results**

* **Primary Endpoint – LDL Cholesterol Reduction:**
  + **Novostatin Arm:**
    - Mean Percentage Reduction: 16.5% (Standard Deviation: 6.2%)
  + **Placebo Arm:**
    - Mean Percentage Reduction: 3.8% (Standard Deviation: 4.5%)
  + **Statistical Significance:** p < 0.001
* **Secondary Lipid Parameters:**
  + **Total Cholesterol:**
    - Reduction of 12% in the Novostatin arm vs. 2% in placebo
  + **HDL Cholesterol:**
    - Slight improvement (increase by 4%) noted in the Novostatin arm
  + **Triglycerides:**
    - Mean reduction of 10% in the Novostatin arm

**4.3 Safety Results**

* **Adverse Events (AEs):**
  + Overall incidence in Novostatin arm: 28% (mild to moderate)
  + Most common AEs: mild headache, transient gastrointestinal discomfort
* **Serious Adverse Events (SAEs):**
  + One SAE (acute allergic reaction) reported in the Novostatin arm; subject recovered after hospitalization.
* **Laboratory Abnormalities:**
  + Minimal elevations in liver enzymes observed in 4 subjects, which resolved following dose adjustments.

**4.4 Pharmacokinetic (PK) Findings (Subset of 50 Subjects)**

* **C\_max:** Mean value of 15.2 ng/mL
* **T\_max:** Approximately 2 hours post-dose
* **AUC:** Consistent with dose-proportional increases

**5. Interim Analysis Discussion**

The interim data indicate a statistically significant reduction in LDL cholesterol in the Novostatin arm compared to placebo, with a mean reduction of 16.5% versus 3.8%, respectively. The improvements in secondary lipid parameters further support the efficacy of Novostatin. Safety data are consistent with the favorable profile observed in earlier studies, with only one serious adverse event reported and managed appropriately. The pharmacokinetic profile confirms the suitability of once-daily dosing.

**6. Interim Analysis Conclusion and Recommendation**

Based on the interim analysis:

* **Efficacy:**  
  The reduction in LDL cholesterol meets the pre-specified efficacy criteria for interim analysis.
* **Safety:**  
  The safety profile remains acceptable, with manageable adverse events.
* **Overall Assessment:**  
  The data support the positive benefit-risk profile of Novostatin.

**Recommendation:**  
It is recommended to continue the trial as planned and to proceed with the planning and initiation of Phase 3 trials upon final analysis. The positive interim outcomes support the advancement of Novostatin to further confirm its efficacy and long-term safety in a larger patient population.

**7. Action Items and Next Steps**

| **Action Item** | **Responsible Party** | **Due Date** | **Status** |
| --- | --- | --- | --- |
| Complete final data collection | Study Sites/EDC Team | September 22, 2024 | Ongoing |
| Final database lock and analysis | Data Management Team | October 20, 2024 | Planned |
| Preparation of final clinical study report | Statistical and Clinical Teams | November 15, 2024 | Planned |
| Submission for Phase 3 planning | Sponsor Regulatory Affairs | December 01, 2024 | Planned |

**8. Signatures**

**Interim Analysis Report Prepared by:**

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Date: July 15, 2024

**Reviewed by:**

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Date: July 16, 2024

**Approved by Investigator:**

Dr. Jane Doe  
Date: July 16, 2024