**Final Clinical Study Report (CSR)**

**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.  
**Investigational Product:** Novostatin (Trade Name: Novitor)  
**CSR Version:** 1.0  
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**1. Executive Summary**

This Final Clinical Study Report (CSR) summarizes the findings from the Phase 2 trial of Novostatin (Novitor), a novel statin designed to treat hypercholesterolemia with the unique advantage of effective lipid lowering at low dosages, thereby reducing the risk of severe side effects. Conducted from March 2, 2024, to September 22, 2024, the trial enrolled 200 subjects randomized in a double-blind, placebo-controlled design. The primary endpoint was the mean percentage change in LDL cholesterol from baseline to Week 24. Secondary endpoints included changes in total cholesterol, HDL cholesterol, triglycerides, and inflammatory biomarkers. The trial demonstrated a statistically significant reduction in LDL cholesterol (mean reduction of 20.5% vs. 4.8% in placebo, p < 0.001) and favorable changes in other lipid parameters. Safety assessments revealed a low incidence of adverse events, with only one serious adverse event that was managed appropriately. The PK/PD, imaging, and biomarker data further support a beneficial cardiovascular profile. Overall, these positive findings support advancing Novostatin into Phase 3 clinical trials.

**2. Introduction**

Hypercholesterolemia is a major risk factor for cardiovascular disease. Statin therapy is a cornerstone of lipid management; however, traditional statins are often limited by dose-dependent side effects, including myopathy and liver enzyme elevations. Novostatin (Novitor) has been developed to address these limitations by achieving effective cholesterol lowering at low dosages. The objective of this Phase 2 study was to evaluate the safety, efficacy, pharmacokinetics, and pharmacodynamics of Novostatin in patients with hypercholesterolemia.

**3. Study Objectives**

**Primary Objective**

* To assess the mean percentage change in LDL cholesterol from baseline to Week 24 in subjects treated with Novostatin compared to placebo.

**Secondary Objectives**

* To evaluate changes in total cholesterol, HDL cholesterol, and triglyceride levels.
* To assess the safety and tolerability of Novostatin, including the incidence of AEs and SAEs.
* To characterize the pharmacokinetic profile of Novostatin.
* To explore pharmacodynamic effects on inflammatory biomarkers (hs-CRP, IL-6) and vascular imaging endpoints (carotid intima-media thickness).

**4. Study Design and Methods**

**4.1 Study Design**

This was a multicenter, randomized, double-blind, placebo-controlled Phase 2 trial. Subjects were randomized in a 1:1 ratio to receive either Novostatin 10 mg once daily or a matching placebo for 24 weeks.

**4.2 Patient Population**

* **Inclusion Criteria:**  
  Adult subjects (18–75 years) with hypercholesterolemia (LDL ≥ 130 mg/dL) despite dietary and lifestyle modifications.
* **Exclusion Criteria:**  
  History of severe statin intolerance, significant liver or renal dysfunction, and recent cardiovascular events.

**4.3 Treatment Regimen**

Subjects received either Novostatin 10 mg or placebo once daily. The treatment period lasted 24 weeks with scheduled visits at baseline, Weeks 4, 12, and 24. An end-of-study follow-up occurred 4 weeks after the final dose.

**4.4 Assessments and Endpoints**

* **Efficacy Assessments:**  
  Lipid profiles (LDL, total cholesterol, HDL, triglycerides), measured at baseline and follow-up visits.
* **Safety Assessments:**  
  Adverse event monitoring, vital signs, ECGs, and laboratory tests (liver enzymes, CK, renal function).
* **PK/PD Assessments:**  
  Blood samples collected for PK analysis and evaluation of inflammatory biomarkers.
* **Imaging Assessments:**  
  Carotid ultrasound for measurement of carotid intima-media thickness (CIMT).

**5. Study Conduct**

**5.1 Enrollment and Randomization**

A total of 200 subjects were enrolled and randomized across 10 study sites. The enrollment process was documented in the subject screening logs, and informed consent was obtained from all participants.

**5.2 Data Collection and Monitoring**

Data were collected using electronic case report forms (eCRFs) and monitored regularly to ensure compliance with the protocol and GCP guidelines. A central data management team oversaw query resolution and data cleaning.

**6. Efficacy Results**

**6.1 Primary Endpoint – LDL Cholesterol Reduction**

**Table 1.** Mean Percentage Change in LDL Cholesterol from Baseline to Week 24

| **Treatment Group** | **n** | **Baseline LDL (mg/dL)** | **Mean % Change in LDL** | **SD (%)** | **p-value** |
| --- | --- | --- | --- | --- | --- |
| Novostatin (Novitor) | 100 | 160.0 ± 15.0 | -20.5% | 6.0 | < 0.001 |
| Placebo | 100 | 158.0 ± 16.0 | -4.8% | 4.5 | – |

A significant reduction in LDL cholesterol was observed in the Novostatin group compared to placebo (20.5% vs. 4.8%, p < 0.001).

**6.2 Secondary Endpoints**

**Table 2.** Changes in Lipid Parameters at Week 24

| **Parameter** | **Novostatin (Novitor)** | **Placebo** | **Between-Group Difference** | **p-value** |
| --- | --- | --- | --- | --- |
| Total Cholesterol | -15.0% ± 5.5% | -3.5% ± 3.8% | -11.5% | < 0.001 |
| HDL Cholesterol | +5.0% ± 2.5% | +1.0% ± 1.8% | +4.0% | 0.002 |
| Triglycerides | -12.0% ± 4.0% | -2.0% ± 3.0% | -10.0% | < 0.001 |

Novostatin significantly improved total cholesterol, increased HDL cholesterol, and reduced triglycerides compared to placebo.

**7. Safety Results**

**7.1 Adverse Events (AEs) and Serious Adverse Events (SAEs)**

**Table 3.** Summary of AEs and SAEs

| **AE/SAE Type** | **Novostatin (n = 100)** | **Placebo (n = 100)** |
| --- | --- | --- |
| Any AE | 28% | 22% |
| Mild AEs | 20% | 18% |
| Moderate AEs | 8% | 4% |
| Serious AEs (SAEs) | 1 (1.0%) | 0 |

The most common AEs in the Novostatin group were mild headache, gastrointestinal discomfort, and muscle cramps. One SAE (acute allergic reaction) was reported in the Novostatin arm and resolved with appropriate medical intervention.

**7.2 Laboratory Assessments**

* **Liver Function Tests:**  
  No clinically significant elevations in ALT or AST were observed; a slight reduction was noted.
* **Muscle Enzymes:**  
  CK levels remained stable, indicating a low risk of myopathy.
* **Renal Function:**  
  Serum creatinine and BUN levels were unchanged from baseline.

**8. Pharmacokinetic/Pharmacodynamic (PK/PD) Findings**

**8.1 Pharmacokinetics**

**Table 4.** Key PK Parameters of Novostatin (n = 50)

| **Parameter** | **Day 1** | **Week 12 (Steady State)** |
| --- | --- | --- |
| C\_max (ng/mL) | 14.8 ± 3.2 | 15.2 ± 3.0 |
| T\_max (hours) | 2.0 (median) | 2.0 (median) |
| AUC\_0–24 (ng·h/mL) | 180 ± 45 | 185 ± 40 |
| t\_1/2 (hours) | 11.5 ± 2.1 | 11.8 ± 2.0 |

Novostatin demonstrated rapid absorption with a consistent PK profile supporting once-daily dosing.

**8.2 Pharmacodynamics**

**Table 5.** Changes in Inflammatory Biomarkers

| **Parameter** | **Novostatin (n = 100)** | **Placebo (n = 100)** | **Between-Group Difference** | **p-value** |
| --- | --- | --- | --- | --- |
| hs-CRP (mg/L) | -25% (3.2 → 2.4) | -5% (3.1 → 3.0) | -20% | < 0.001 |
| IL-6 (pg/mL) | -15% (4.5 → 3.8) | -2% (4.6 → 4.5) | -13% | 0.001 |

The PD data indicate significant reductions in inflammatory biomarkers, supporting a beneficial effect on cardiovascular risk.

**9. Imaging and Biomarker Findings**

**9.1 Imaging (Carotid Ultrasound)**

**Table 6.** Carotid Intima-Media Thickness (CIMT)

| **Parameter** | **Novostatin (n = 80)** | **Placebo (n = 80)** | **Between-Group Difference** | **p-value** |
| --- | --- | --- | --- | --- |
| Baseline CIMT (mm) | 0.90 ± 0.10 | 0.92 ± 0.11 | — | — |
| Week 24 CIMT (mm) | 0.85 ± 0.09 | 0.91 ± 0.10 | -0.06 mm | 0.002 |

A significant reduction in CIMT was observed in the Novostatin group compared to placebo, suggesting an impact on vascular health.

**10. Discussion**

The Phase 2 trial of Novostatin (Novitor) demonstrated a robust efficacy profile with a significant reduction in LDL cholesterol and other lipid parameters, accompanied by improvements in inflammatory biomarkers and vascular imaging outcomes. The PK data support the once-daily dosing regimen, and the safety profile was favorable with only minimal adverse events. The integrated data suggest that Novostatin not only effectively lowers cholesterol but may also confer additional cardiovascular protection by reducing systemic inflammation and slowing atherosclerotic progression.

**11. Conclusion and Recommendations**

The results from this Phase 2 study provide compelling evidence of the efficacy and safety of Novostatin (Novitor) in patients with hypercholesterolemia. Key findings include:

* A statistically significant reduction in LDL cholesterol (−20.5% vs. −4.8% with placebo).
* Favorable improvements in total cholesterol, HDL cholesterol, and triglycerides.
* A positive PK/PD profile and significant reductions in inflammatory biomarkers.
* A reduction in carotid intima-media thickness, indicating potential vascular benefits.
* An acceptable safety and tolerability profile with minimal adverse events.

**Recommendation:**  
Based on these positive outcomes, it is recommended to proceed to Phase 3 clinical trials to further confirm the efficacy and safety of Novostatin in a larger patient population.

**12. Appendices**

* **Appendix A:** Informed Consent Forms
* **Appendix B:** Protocol Deviation Logs
* **Appendix C:** Detailed Statistical Analysis and Data Listings
* **Appendix D:** Central Laboratory Reports and Quality Control Data
* **Appendix E:** Imaging Core Laboratory Report

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