Phase Ib Study of Icosabutate, A Novel Structurally Enhanced Fatty Acid, in Subjects with Hypercholesterolemia

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• INTRODUCTION:
Icosabutate, an orally active structurally enhanced fatty acid (SEFA), has demonstrated reduction in triglycerides (TG) and cholesterol in several rodent models of dyslipidemia and diabetes. In clinical single and multiple dose studies icosabutate was well tolerated and significantly lowered LDL-C, non-HDL-C and TG in subjects with mixed dyslipidemia.

• AIM:
This phase 1b study explored the lipid lowering effects of icosabutate in subjects with hypercholesterolemia.

• METHODS:
Randomized double blind, placebo controlled study of icosabutate 600 mg OD. Subjects with hypercholesterolemia treated with a statin for at least 3 months were screened (Figure 1). Statins were temporarily withdrawn from statin, 28 days treatment with icosabutate or placebo (n=18) or placebo (n=6). Baseline lipid values were well-balanced between the groups (Table 1). Efficacy results are shown in Figures 2-6. Icosabutate significantly reduced TG, non-HDL-C, LDL-C, Total-C, apo B compared to placebo. Apo C3 was significantly reduced from baseline Day 28. Changes in Lipids and Lipoproteins.

• RESULTS:
24 while, male subjects with an average age of 55 (33-65) and BMI of 27.9 kg/m2 (24.7-32.2) were randomized to icosabutate, 600 mg OD, (n=18) or placebo (n=6). Baseline lipid values were well-balanced between the groups (Table 1). Efficacy results are shown in Figures 2-6. Icosabutate significantly reduced TG, non-HDL-C, LDL-C, Total-C, apo B compared to placebo. Apo C3 was significantly reduced from baseline and PCSK-9 was significantly increased compared to placebo.

• COMMENT TO VALUES:
There is a slight variance in values presented in the abstract and those presented in this poster – The values in the abstract are reported as median percentage change from baseline (average of visit 2-6) to 24 hours after last dose (day 28). – The values in this poster are reported in line with the clinical study report as % mean change from baseline (day-1) to day 28.

• SAFETY:
The number of subjects reporting adverse events (AEs) were balanced between the treatment arms (Table 2). There were no other findings of clinical importance in the clinical laboratory evaluations, vital signs, 12-lead ECGs, telemetry, physical examinations, or body weight observed during the study.

• CONCLUSION:
In this exploratory phase 1b study in hypercholesterolemic subjects temporarily withdrawn from statins, 28 days treatment with icosabutate showed promising results

ICOSABUTATE:
• Reduced Total-C, LDL-C, non-HDL-C, TG, and apo B compared to placebo
• Reduced plasma apo C3 substantially from baseline
• Increased plasma PCSK-9 levels compared to placebo
• Appeared safe and well tolerated

The results extend and confirm pre-clinical data on icosabutate and suggest a unique pharmacological profile with large, robust reductions in both LDL-C and TGs. These exploratory data indicate that icosabutate may be an important novel lipid-lowering agent in several patient populations. The results await confirmation in designated efficacy studies.

• AUTHOR’S DISCLOSURE:
This study was in whole sponsored by Pronova BioPharma Norge AS – part of BASF. Authors not employed by Pronova BioPharma/BASF have no conflict of interest.