Results of a 52 week Open-Label Phase 2b Study to Assess Long-term Safety, Immunogenicity and LDL-C Efficacy of Monthly Dosing With LIB003 a novel anti-PCSK9 recombinant fusion protein

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Disclosure/Conflict of Interest: Dr Turner’s institution has received research funding from LIB Therapeutics, Amgen, Medicine Co/Novartis, Regeneron/Sanofi, CiVi and Pfizer

ClinicalTrials.gov Identifier: NCT03847974

88TH EAS CONGRESS
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Oct 04-07, 2020

Study Design

Patients who had completed the Phase 2 LIB003-002 trial and met eligibility criteria → Open-label extension (52 weeks/12 months): LIB003 300 mg subQ Q4W

	W0	W4	W8	W12	W16	w20	W24	W28	W32	W36	W40	W44	W48	W52
Assessments	M0	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11		M12

Patient Characteristics

- 32 (40%) patients completing the 12-week Phase 2 dose-ranging trial entered this Phase 2b OLE trial
- 28 (~88%) had been on LIB003; (enrollment limitation was due to availability of drug)

Number of patients	**32**
Age (years): Mean (range)	**63.1 (32-80)**
Sex (%): Male/female	**37.5/62.5**
Race (%): White/Black	**78/22**
BMI (kg/m2): Mean (SD)	**30.08 (4.608)**
CVD	**28%**
Diabetes	**44%**
FH	**31%**
Statin use (%): High intensity/Mod-Low/None	**56.3/28.1/15.6**
Ezetimibe use (%)	**25.0**
Baseline LDL-C (Friedewald) (mg/dL) Mean (SD)	**124.3 (40.29)**
Minimum/Maximum	78/297
Baseline apo B (mg/dL) mean (SD)	**99.8 (24.58)**
Minimum/Maximum	73/198
Baseline Lp(a) (nmol/L): Median (SD)	**76.5 (132.04)**
Minimum/Maximum	5-518

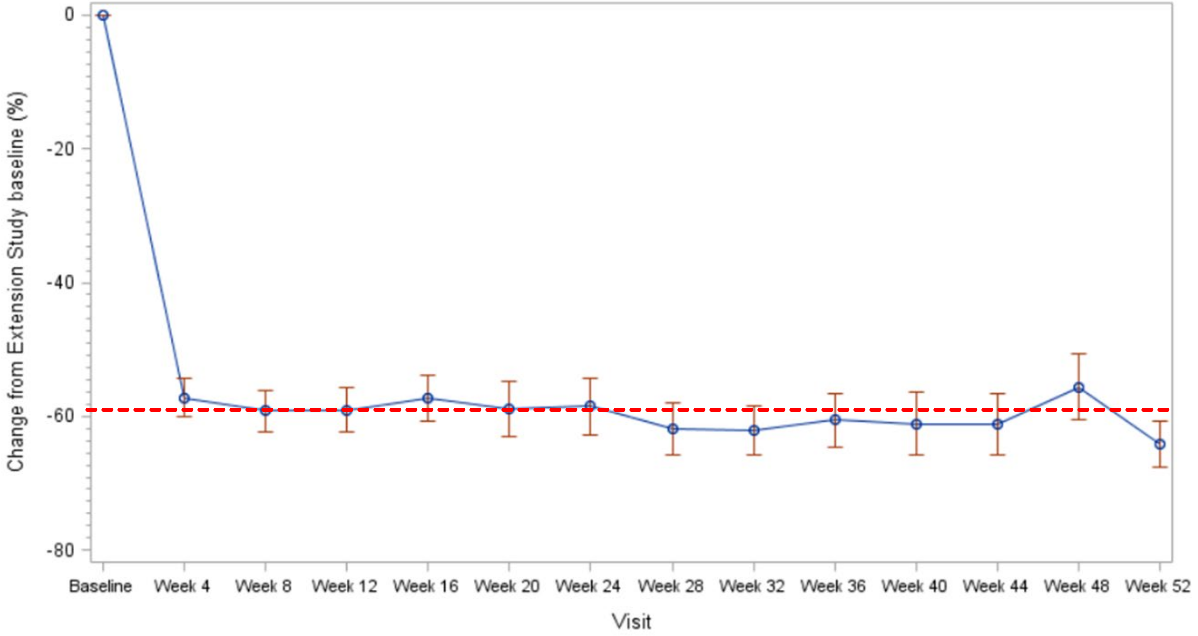
LIB003 Open-label Extension Phase 2b Study

LDL-C Efficacy

Mean (±SE) % Change From OLE Baseline in LDL-C (Friedewald) at week 52 – ITT Population

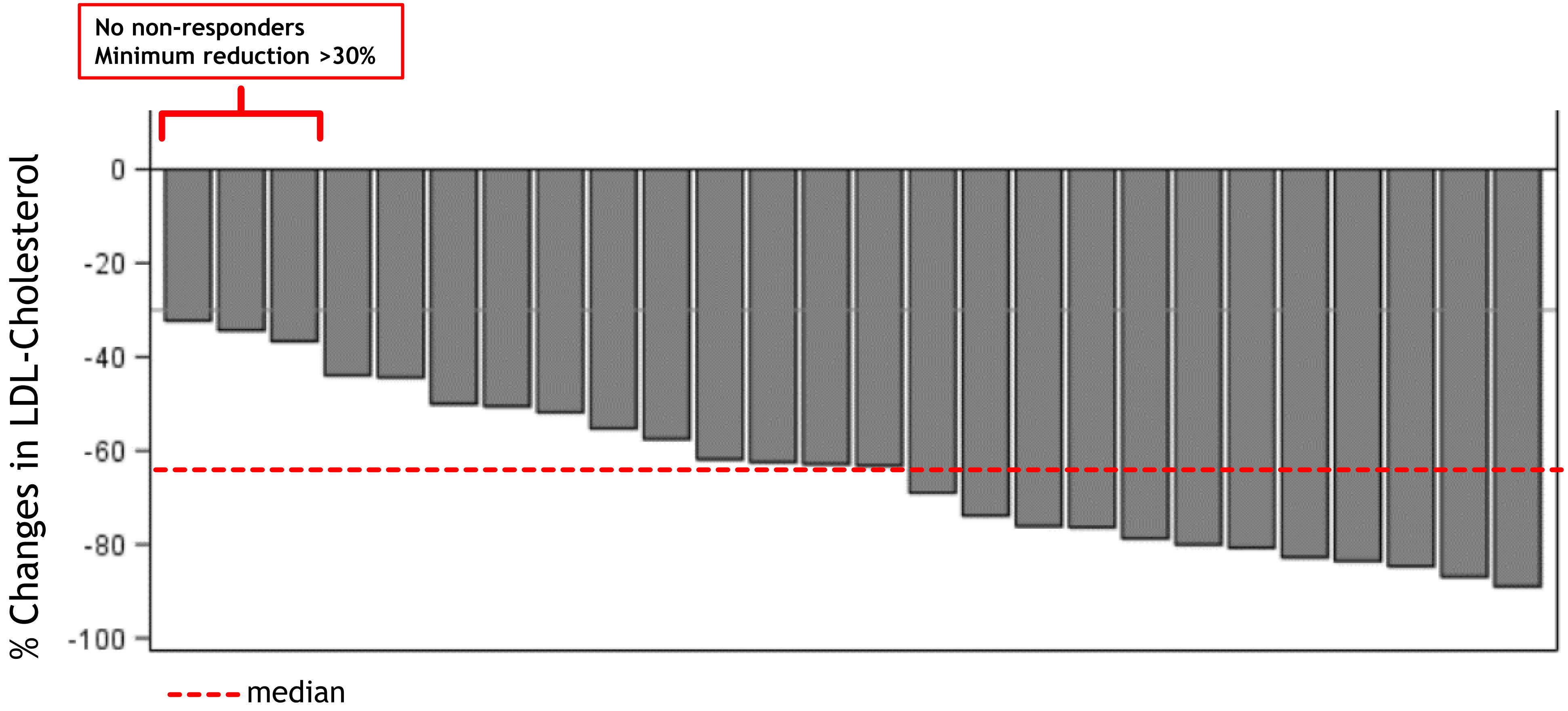
Baseline (n)	**32**
Mean LDL-C (SD) mg/dL	124.3 (40.29)
Week 52 (n)	26
% Change from Baseline: mean (SD)	-64.1 (17.38)
95% CI	(-71.2, -57.1)
P-value	<0.0001

LDL-C (Friedewald) by week: Mean (SE) % change from OLE baseline



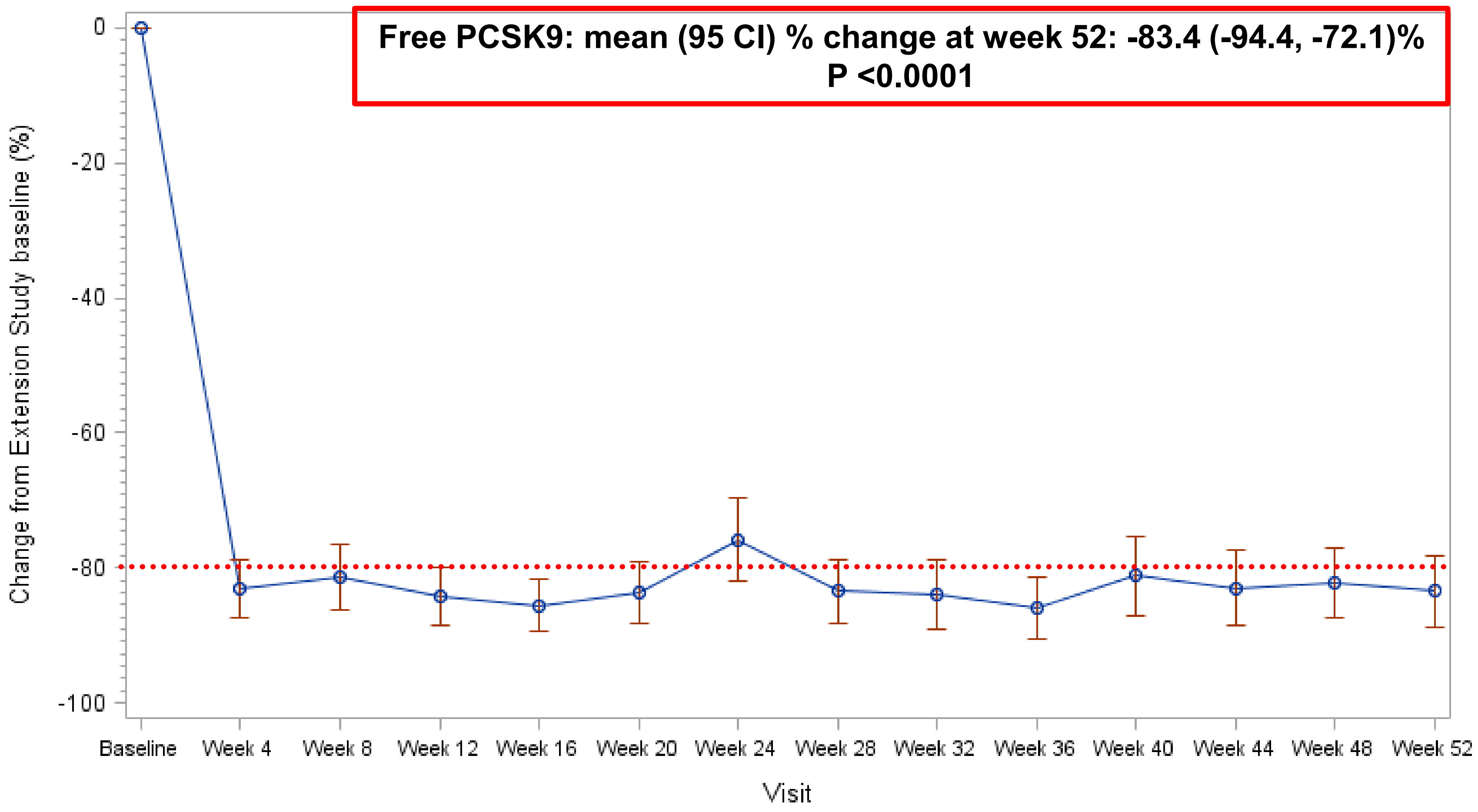
LIB003 Open-label Extension Phase 2b Study: LDL-C Efficacy

Waterfall Plot - ITT: % Changes in LDL-C by Friedewald Formula from baseline to week 52



LIB003 Open-label Extension Phase 2b Study: PCSK9 Efficacy

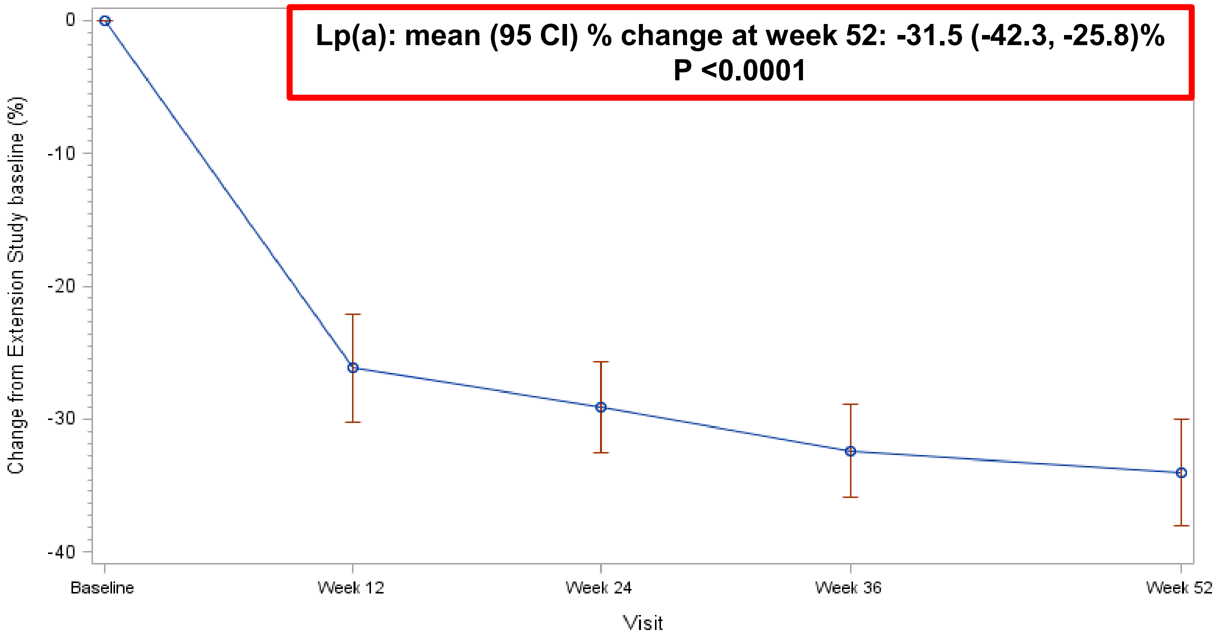
Mean (±SE) % Change From OLE Baseline in Free (unbound) PCSK9 by Visit - ITT Population



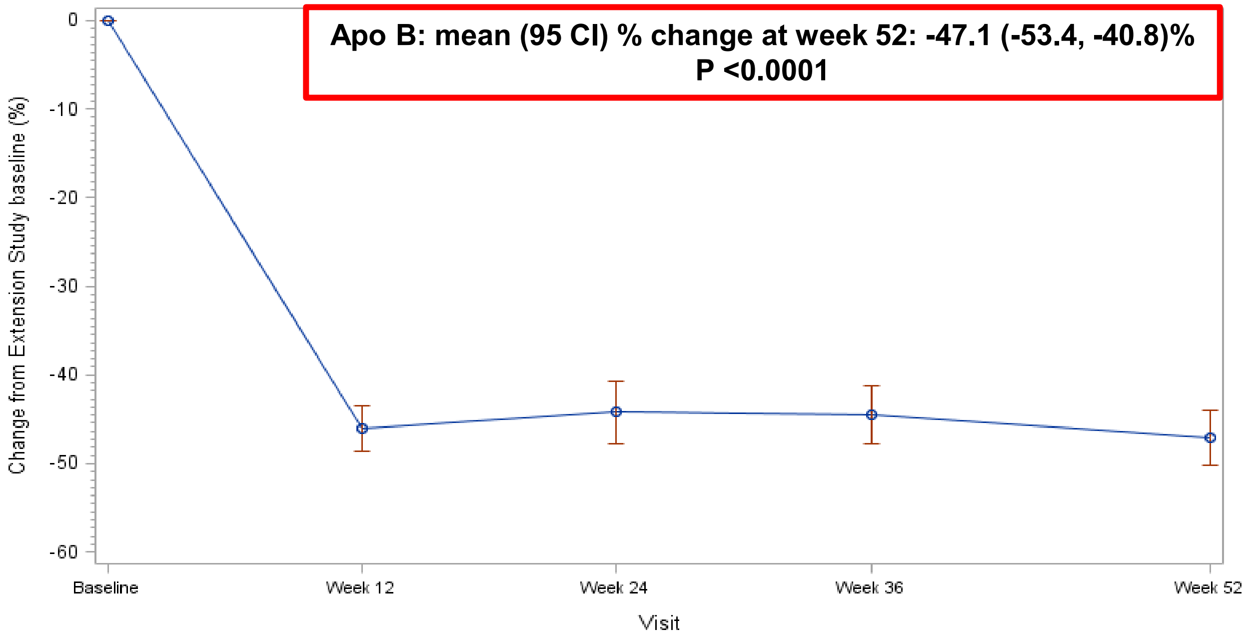
LIB003 Open-label Extension Phase 2b Study: Apolipoproteins

Lp(a) and Apo B changes through week 52 - ITT analysis

Lipoprotein (a): baseline median 131.8 mmol/L



Apolipoprotein B: baseline mean 99.8



LIB003 Open-label Extension Phase 2b Study: Safety Analysis

- **Patient disposition:**
  - 26 patients completed the trial; 5 patients withdrew due to non-study related reasons (e.g. relocation or unable to keep visits), 1 patient withdrew due to AE of shoulder pain
  - 27 (80%) of patients completed the trial with 12 or 13 doses and 90% received >9 doses
- **Clinical:**
  - SAE: 3 events (small bowel obstruction; worsening of uterine fibroids; supraventricular tachycardia) all considered by PI as unrelated to study drug
  - AE: 63 events (38 mild, 25 moderate) – none related to study drug by PI
  - ISR: 5 patients at single visit (1.4% of all doses received) all considered mild (erythema, swelling, induration and/or itching)
- **Laboratory: No trends or significant increases in any parameters**
  - Hepatic transaminases – nil >2 x ULN
  - CK – nil >3 x ULN unless exercise related
- **ADAs:**
  - Low level of ADAs ***not associated with any safety signals or ISRs***
  - Transient Nab tests in 2 pts with no effect on ISRs, free PCSK9 or LDL-C efficacy; 1 pt Nab disappeared with continued dosing and free PCSK9 and LDL-C reductions were 99% and 79% respectively at week 52. The 2nd pt had +ve Nab at week 52, along with free PCSK9 reduced by 67% and LDL-C by 32%, consistent with values at other earlier visits. Nab was -ve on 4-week follow-up. After amendment pt received LIB003 for 12 more weeks with no Nab detected and free PCSK and LDL-C reductions of 59-85% and 31-42% respectively

LIB003: Results Of Open-label Extension Phase 2b Study

Summary and Conclusions

- LIB003 300 mg SC Q4W for 52 weeks in an OLE trial, with an additional 12 weeks in 88% of patients in the phase 2 trial for 64 weeks exposure, was well tolerated and showed no unexpected or significant adverse clinical or laboratory safety signals.
- ISRs were infrequent and mild
- Stable mean LDL-C reductions of >64% based on ITT analysis
- Free PCSK9 suppression was maintained at >80% at trough
- Low levels of ADAs were seen with 2 transitory NAbs with ***no impact*** of LDL-C, free PCSK9 or association with ISRs
- Larger and longer Phase 3 trials with LIB003, 300 mg Q4W in 1 mL, are in progress to fully assess safety and efficacy of this novel highly efficacious Q4W anti-PCSK9 therapeutic.