The STAM™ NASH model in diabetic C57BL/6J mice fed a high fat diet (Fujii M. et al. 2013), is reproducible and follows a predictable path of steatosis, hepatic inflammation, hepatocellular ballooning degeneration, fibrosis and HCC (hepatocellular carcinoma).

**Results Continued**

### Hepatocellular ballooning

- **Vehicle:** No ballooning
- **SOLI 50 mg/kg QD:** Mild ballooning
- **SOLI 100 mg/kg QD:** Moderate ballooning

### Lobular inflammation

- **Vehicle:** No inflammation
- **SOLI 50 mg/kg QD:** Mild inflammation
- **SOLI 100 mg/kg QD:** Moderate inflammation

### Steatohepatitis Score

- **Vehicle:** No damage
- **SOLI 50 mg/kg QD:** Mild damage
- **SOLI 100 mg/kg QD:** Moderate damage

The 50 mg/kg QD dose showed the greatest effect, while the 5 mg/kg/day (QD) dose had no effect. There was no increased benefit at the 100 mg/kg QD dose. In order to determine the effect on fibrosis and HCC that reproducibly occurs in the mouse model, the experiment was repeated with treatment initiated from 4-8 weeks after birth (4 weeks of treatment) and 8-12 weeks after birth (4 weeks of treatment). mRNA expression levels for glucose-6-phosphatase and fructose-1,6-bisphosphatase, two enzymes involved in gluconeogenesis, were suppressed.

### Effect on Fibrosis

The fibrosis area and the tumor nodules (both size and number) were significantly decreased in the SOLI treated group.

### Size and Number of Visible Tumor Nodules

- **Vehicle:** 103.7 (n=8)
- **SOLI 50 mg/kg QD:** 57 (n=8)
- **SOLI 100 mg/kg QD:** 25 (n=8)

### Conclusions

- **SOLI** was effective in reducing NASH and significantly reduced NAFLD scores in a diabetes and high fat diet induced NASH mouse model.
- **SOLI** produced statistically significant reduction in inflammation, hepatocellular ballooning degeneration, fibrosis, and HCC at a daily dose that is equivalent or lower than the HED that has been well tolerated and effective in two global Phase 3 trials to treat moderate to moderately severe CAGB.
- **SOLI** was effective in reducing blood glucose, without significant improvement in insulin levels in the NASH mice.
- **SOLI** does not have activity against anaerobic Gram-negative intestinal microflora. Therefore, the anti-NASH activity is not believed to occur as a result of SOLI's 1,6-bisphosphatase and glucose-6-phosphatase in the liver.
- The availability of a large safety database and the data in the NASH mouse model support exploratory development of SOLI for the treatment of NAFLD and NASH in humans.
- An exploratory trial in patients with biopsy-proven NASH is currently underway.

### Disclosures

P. Fernandes and D. Oldach are employees of Cempra and receive compensation in salary and option share. P. Gholam is a paid consultant for Cempra. T. Hashiguchi, Y. Shirakata, and H. Yoneyama work at the Stellic Institute in Tokyo, Japan and this work was paid for under contract to Stellic.