1. Background – Hepatitis Delta

- HDV leads to the most severe form of viral hepatitis
  - More rapid progression to liver cirrhosis
  - More likely to develop HCC / decompensation vs HBV
- HDV is always associated with HBV infection
  - HDV steals HBsAg from HBV from envelopment
- Final step in replication involves prenylation
  - HDV hijacks prenylation, a host process
- No FDA approved Rx for HDV
  - PEG IFN-a demonstrates modest benefit
- HDV worldwide prevalence is 15 - 20 million
- Approximately 4-6% of HBV worldwide population is infected with HDV
- Orphan status in US and EU

2. Background - Lonafarnib

- Lonafarnib is a small molecule, oral, prenylation inhibitor
- Well-characterized through Phase 3
  - >2,000 patients dosed in oncology program by Merck
  - Dose limiting toxicity is GI (class effect)
- Lonafarnib extensively metabolized by CYP3A4
- Co-dosing with Ritonavir (CYP3A4 inhibitor) has:
  - Demonstrated 4-5 fold increase in lonafarnib serum levels
  - Enabled use of low dose lonafarnib with higher post-absorbed drug levels, leading to improvement in GI tolerability

3. Program Design – The LOWR HDV Program

- LOWR HDV - 3 “QD” Study
  - N = 21
- LOWR HDV - 2 “Dose-Finding” Study
  - N = 46
- LOWR HDV - 4 “Dose-Escalation” Study
  - N = 45

- LOWR HDV (Lonafarnib With Ritonavir in HDV) Program
  - Identifying dose and regimen for registration study
- Over 100 HDV patients dosed across international sites

4. Methods

- Purpose
  - To identify optimal combination regimens of LNF and RTV + PEG IFN-α which demonstrate efficacy and tolerability for longer term dosing to enable HDV RNA clearance.

- Patients and Methods
  - Treatment duration 12-24 weeks
  - 72 hour PK and PD evaluation on day 1 and day 28
  - Testing frequency: days 1, 2, 3, 7, 14, 28 and then Q4W
    - Biochemical parameters
    - HDV-RNA (by quantitative real-time PCR)

5. Study Design

6. Results

- LNF 25 mg BID + RTV 100 mg BID
  - 3 of 5 (60%) become HDV-RNA PCR-negative at Week 24
  - 5 of 5 (100%) achieve HDV-RNA BLOQ at Week 24

- LNF 25 mg BID + RTV + PEG IFN-α 180 mg QW
  - 60% of Patients Normalized ALT at Week 24*

7. Conclusions

- Antiviral activity demonstrated in all LOWR HDV – 2 patients
- LNF 25 mg and 50 mg BID based regimens demonstrate improved GI tolerability
  - Longer dosing may now be possible and necessary
- LNF 25 mg BID + RTV + PEG IFN demonstrates most rapid and profound VL decline
  - 3 of 5 (60%) become HDV-RNA PCR-negative at Week 24
  - 5 of 5 (100%) achieve HDV-RNA BLOQ at Week 24
  - Dosing > 6 months may improve outcomes (HDV-RNA PCR-negativity)
- 60% patients normalized ALT at Week 24
- LNF 50 mg BID + RTV leads to 18% HDV-RNA PCR-negativity on-treatment
  - Further studies with all oral therapy are warranted
- Mostly grade 1 GIs AEs observed with lower doses

8. References

1. Carl K et al. Jantaki Intra Di 2015; 5 915-917
3. LOWR HDV Program
4. LOWR HDV – 2: “Dose Finding” Study
5. LOWR HDV – 4: “Dose Escalation” Study

9. Disclosures

Lonafarnib was provided by Eiger BioPharmaceuticals, Inc. Glenn: Equity interest in Eiger BioPharmaceuticals, Inc.
Yurdaydin: Travel support from Eiger BioPharmaceuticals, Inc. All other authors have no financial disclosures.