



## **Eiger Announces Positive Phase 2 Data at the American Association for the Study of Liver Diseases (AASLD) Meeting: Multiple Paths Forward Identified with Lonafarnib Therapy in LOWR HDV Program**

**- Data Presented through Monday Morning**

PALO ALTO, Calif., Nov. 14, 2016 /PRNewswire/ -- Eiger BioPharmaceuticals, Inc. (NASDAQ: EIGR) today announced an update on presentations of data from its LOWR HDV (**L**onafarnib **W**ith **R**itonavir in **H**epatitis **D**elta **V**irus) Program presented as of today at the American Association for the Study of Liver Diseases (AASLD) meeting in Boston, Massachusetts. LOWR HDV is a multi-center, international Phase 2 program designed to identify optimal dosing of lonafarnib (LNF) with ritonavir (RTV) ± pegylated interferon (PEG IFN) for development in the treatment of hepatitis delta infection (HDV).



### **Key Findings:**

- LNF + RTV (all-oral) regimens achieve HDV-RNA PCR-negativity on treatment
- Low dose LNF + RTV with PEG IFN achieves the most rapid and profound viral load decline, with the highest rate of HDV-RNA PCR-negativity on treatment
- LNF + RTV based regimens lead to normal ALT
- Gastrointestinal adverse events were predominantly mild or moderate
- LNF based regimens can induce a reactivation of the immune response to HDV leading to post-treatment viral clearance of HDV-RNA and reversal of fibrosis

The company will discuss clinical and regulatory plans later today at the LOWR HDV Program Analyst Event in Boston.

### **Lonafarnib Presentations at AASLD: Through this morning (November 14):**

#### **LOWR HDV – 2 "Dose-Finding" Study**

*Yurdaydin, C. et al; "Exploring Optimal Dosing of Lonafarnib with Ritonavir for the Treatment of Chronic Delta Hepatitis." Abstract #1845, Poster.*

LOWR HDV – 2 is a dose-finding study to identify optimal combination regimens of LNF and RTV ± PEG IFN, with efficacy and tolerability for long-term dosing to enable HDV-RNA clearance. In this open-label study, 46 HDV-infected patients have been enrolled to date into 9 groups of different doses of LNF in combination with RTV ± PEG IFN for dosing durations of 12 or 24 weeks. LNF doses range from 100 mg twice daily (BID) to 25 mg BID. LOWR HDV – 2 is being conducted at Ankara University in Ankara, Turkey.

Results from LOWR HDV – 2:

- LNF 25 mg BID + RTV + PEG IFN (triple therapy) leads to best response rate
  - 3 of 5 (60%) become HDV-RNA PCR-negative at week 24
  - 5 of 5 (100%) below limit of HDV-RNA quantification on treatment
- Dosing > 6 months may improve outcomes (HDV-RNA PCR-negativity)
- 60% of patients normalized ALT
- LNF 50 mg BID + RTV (all oral) leads to 2 of 11 (18%) HDV-RNA PCR-negativity
  - Further studies of all-oral therapy are warranted
- LNF 25 mg and 50 mg BID based regimens are generally well tolerated
  - Mostly grade 1 GI (gastrointestinal) AEs observed with LNF 25 and 50 mg BID based regimens
  - Longer dosing now possible

"Data from the LOWR HDV – 2 triple therapy arm with LNF 25 mg BID, RTV, and PEG IFN have generated promising results at

24 weeks, and demonstrate an exciting synergy between LNF and PEG IFN. As with Hepatitis C, if we can continue to treat while patients remain HDV-RNA PCR-negative for an additional 24 weeks, I expect this can maximize the percentage of patients who will remain PCR-negative off-treatment," said Cihan Yurdaydin, MD, Principal Investigator, Chair of the Department of Gastroenterology and Chief of the Hepatology Institute at the University of Ankara, in Turkey. "Importantly, in the LOWR HDV – 2 study, we have now identified the correct low dose LNF regimens that are well tolerated, which will support such a pivotal 48 week treatment study."

In addition, Dr. Yurdaydin said, "We have identified optimal all-oral combinations of LNF + RTV that are well tolerated and retain antiviral efficacy. This has enabled patients to achieve HDV-RNA PCR-negativity on-treatment, and exemplifies the first all-oral regimen for HDV patients. There appears to be multiple options for exploration of LNF in HDV infection in the future, including all-oral regimens, for longer durations."

### **Observation of Post-Treatment Viral Clearance in LOWR HDV Program**

*Yurdaydin, C. et al; "The Prenylation Inhibitor Lonafarnib Can Induce Post-Treatment ALT Flares with Viral Clearance in Patients with Chronic Delta Hepatitis." Abstract #1875, Poster.*

Twenty-seven patients who had detectable HDV RNA after receiving LNF for 12 or 24 weeks in the LOWR HDV – 1 and LOWR HDV – 2 trials were followed. Observations included post-treatment ALT flares followed by HDV-RNA PCR-negativity with HBV-DNA decline. A post-treatment ALT flare was defined as elevation of ALT to >2x baseline ALT level. Post-treatment analysis of LOWR HDV – 1 and LOWR HDV – 2 is being conducted at Ankara University in Ankara, Turkey.

#### **Summary of Results:**

- LNF-induced immune reactivation in HDV-infected patients may be a mechanism for viral clearance
- Post-treatment ALT flares observed in a subset of HDV-treated patients
  - 5 of 27 (18.5%) patients experienced post-treatment flares
- Immune reactivation with post-treatment ALT flares followed by:
  - HDV-RNA PCR-negativity (5/5 patients)
  - Normalized ALT levels (4/5 patients)
  - HBV-DNA decline (4/5 patients)
  - Change in HBsAg from 3,927 IU/mL (baseline) to 5 IU/mL (1/5 patients)
- Novel observation (vs. prior IFN studies) in HDV
- Long term ALT normalization has resulted in reversal of fibrosis
- One patient experienced transient hyperbilirubinemia associated with the ALT flare, followed by HBsAg decrease to less than 10 IU/mL, ALT normalization, and HDV-RNA PCR-negativity

"We are excited to observe this novel phenomenon of post-treatment ALT flares followed by HDV-RNA PCR-negativity. The data suggest that a short course of LNF may contribute to an effective reset and activation of the immune reactivity to HDV, which in some cases may spread to HBV," said Jeffrey Glenn, Associate Professor of Medicine, and Microbiology and Immunology, Stanford School of Medicine. "Thus, there may be at least two pathways for achieving HDV negativity with LNF therapy. The first is the on-treatment LNF-induced progressive suppression to HDV negativity with ALT normalization, which is the more classical antiviral approach as exemplified in the ongoing LOWR HDV - 2 study. The second pathway is LNF-induced post-treatment anti-HDV ALT flares. We look forward to reviewing additional post-treatment data from the ongoing studies in the LOWR HDV Program to better understand the frequency by which this phenomenon may be observed."

### **LOWR HDV – 3 "QD Dosing" Study**

*Koh, C. et al; Exploring Once Daily Dosing of Lonafarnib with Ritonavir for the Treatment of Chronic Delta Hepatitis." Oral Presentation at 12<sup>th</sup> Hepatitis Delta International Network (HDIN) Meeting.*

LOWR HDV – 3 is a double-blind, randomized, placebo-controlled study designed to evaluate the efficacy and tolerability of once-daily doses of LNF – 50 mg, 75 mg and 100 mg – each combined with RTV 100 mg once daily for 12 (N=9) or 24 (N=12) weeks. Twenty-one patients with chronic hepatitis delta were randomized into one of six treatment groups. LOWR HDV – 3 is being conducted at the National Institutes of Health (NIH) Bethesda, MD, and dosing has completed.

#### **Results from LOWR HDV – 3:**

- Mean log HDV-RNA change of -1.93, -1.30, -0.29 for LNF 50 mg, 75 mg, 100 mg QD, respectively, at week 24
- Mean log HDV-RNA change of -1.54 in responders (N=7) versus -0.11 in non-responders (N=5) at week 24 ( $p < 0.0001$ )
- Viral load declines correlated with LNF serum concentration ( $p = 0.003$ )
- Once daily (QD) LNF dosing did not achieve on-treatment HDV-RNA PCR-negativity by week 24, although 1/4 (25%) of

patients in each arm had steady declines of HDV-RNA throughout the treatment period (-5.67 log, -4.87 log, -2.94 log)

- Although most patients are still in early follow-up, one patient has become HDV-RNA PCR-negative post-treatment
- LNF + RTV was generally well tolerated at all doses
  - Predominantly grade 1, no grade 3 GI AEs

"The NIH Clinical Center previously completed the first proof of concept Phase 2 study involving LNF in HDV-infected patients, and these results were published in *The Lancet Infectious Disease* in 2015," said Christopher Koh, MD, Study Lead and Staff Clinician at the National Institute of Diabetes and Digestive and Kidney Diseases, part of the NIH. "We are pleased to be participating in the LOWR HDV Program to determine optimal dosing of LNF in HDV-infected patients. The LOWR HDV – 3 study enabled us to investigate all-oral, daily (QD) dosing of LNF in combination with RTV. Given the good tolerability and viral load declines in some patients, extending treatment to 48 weeks looks promising. I think the most exciting results may be in the follow-up phase, where we have already seen one patient become HDV-RNA PCR-negative post-treatment."

#### **Lonafarnib Presentations at AASLD: Later Today (November 14):**

- *Wedemeyer, H. et al; "A Phase 2 Study of Titrating-Dose Lonafarnib Plus Ritonavir in Patients With Chronic Hepatitis D: Interim Results From The Lonafarnib With Ritonavir In HDV – 4 (LOWR HDV – 4) Study." Abstract #230, Oral Presentation, Parallel 35: Hepatitis B: Novel Therapies, November 14, 5:00 – 5:15 pm, Sheraton: Back Bay ABC*
- *"Developing a Treatment for HDV: LOWR HDV Program Review". A review of key findings from the Phase 2 LOWR HDV Program, including LOWR HDV – 2, – 3, – 4 studies. Renowned key opinion leaders and principal investigators Cihan Yurdaydin, MD (Ankara University), Heiner Wedemeyer, MD (Hannover Medical School), and Jeffrey Glenn, MD, PhD (Stanford School of Medicine) will review presentations and discuss results. Members of the Eiger executive team will provide an overview of the Company's regulatory plans for its HDV program. November 14, 6:30 – 8:00 pm, Hilton Boston Back Bay, Mariner Room.*

#### **About Sarasar™ (lonafarnib)**

Lonafarnib is a well-characterized, late-stage, orally active inhibitor of farnesyl transferase, an enzyme involved in modification of proteins through a process called prenylation. HDV uses this host cell process inside liver cells to complete a key step in its life cycle. Lonafarnib inhibits the prenylation step of HDV replication inside liver cells and blocks the virus life cycle at the stage of assembly. Since prenylation is carried out by a host enzyme, treatment with lonafarnib may present a higher barrier to development of viral resistance mutations. Lonafarnib has been dosed in over 100 HDV-infected patients across international academic centers and is in Phase 2 development for HDV. Lonafarnib has been granted Orphan Drug Designation by the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA), and Fast Track Designation by U.S. FDA. Lonafarnib is not approved for any indication, and is licensed from Merck Sharp & Dohme Corp. (known as MSD outside of the United States and Canada).

#### **About Hepatitis Delta Virus (HDV)**

Hepatitis Delta (or Hepatitis D) is caused by infection with HDV and is considered to be one of the most severe forms of viral hepatitis in humans. Hepatitis delta occurs only as a co-infection in individuals harboring Hepatitis B Virus (HBV). Hepatitis delta leads to more severe liver disease than HBV alone and is associated with accelerated liver fibrosis, liver cancer, and liver failure. Hepatitis delta is a disease with a significant impact on global health, which may affect up to approximately 15-20 million people worldwide. The prevalence of HDV varies among different parts of the world. Globally, HDV infection is reported to be present in approximately 4.3% to 5.7% of chronic Hepatitis B carriers. The prevalence of HDV in patients infected with chronic HBV is even higher in certain regions, including certain parts of Mongolia, China, Russia, Central Asia, Pakistan, Turkey, Africa, and South America, with an HDV prevalence as high as 60% being reported in HBV-infected patients in Mongolia and Pakistan.

#### **About Eiger**

Eiger is a clinical-stage biopharmaceutical company committed to bringing to market novel products for the treatment of rare diseases. The company has built a diverse portfolio of well-characterized product candidates with the potential to address diseases for which the unmet medical need is high, the biology for treatment is clear, and for which an effective therapy is urgently needed.

#### **Note Regarding Forward-Looking Statements**

This press release contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, included in this press release regarding our strategy, future operations, future financial position, future revenue, projected expenses, prospects, plans and objectives, intentions, beliefs and expectations of management are forward-looking statements. These forward-looking statements may be accompanied by such words as "anticipate," "believe," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "potential," "project," "target," "will" and other words and terms of similar meaning. Examples of such statements include, but are not limited to, whether or not pegylated interferon lambda-1a or lonafarnib or ubenimex or exendin 9-39 may be further developed and the timing of potential additional clinical trials and potential for approval, statements relating to the availability of cash for Eiger's future operations and drug development portfolio, Eiger's

ability to develop its drug candidates for potential commercialization, the timing of the commencement and number and completion of Phase 2 trials and whether the products can be successfully developed or commercialized. Various important factors could cause actual results or events to differ materially from the forward-looking statements that Eiger makes, including the risks described in the "Risk Factors" sections in the Annual Report on Form 10-K for the period ended December 31, 2015 and Eiger's periodic reports filed with the SEC. Eiger does not assume any obligation to update any forward-looking statements, except as required by law.

Investors: Andrew McDonald, LifeSci Advisors, LLC, 646-597-6987, [andrew@lifesciadvisors.com](mailto:andrew@lifesciadvisors.com)

Logo - <http://photos.prnewswire.com/prnh/20151108/285009LOGO>

To view the original version on PR Newswire, visit: <http://www.prnewswire.com/news-releases/eiger-announces-positive-phase-2-data-at-the-american-association-for-the-study-of-liver-diseases-aasld-meeting-multiple-paths-forward-identified-with-lonafarnib-therapy-in-lowr-hdv-program-300361929.html>

SOURCE Eiger BioPharmaceuticals, Inc.

