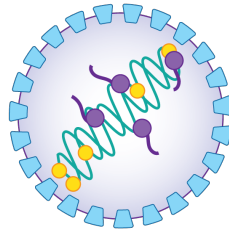




HEPATITIS DELTA VIRUS (HDV)

OVERVIEW

- Most severe form of viral hepatitis
- Always associated with HBV infection
- HDV causes more rapid disease progression
 - Compared to HBV mono-infection
- No FDA approved Rx
 - PEG IFN alpha demonstrates modest benefit



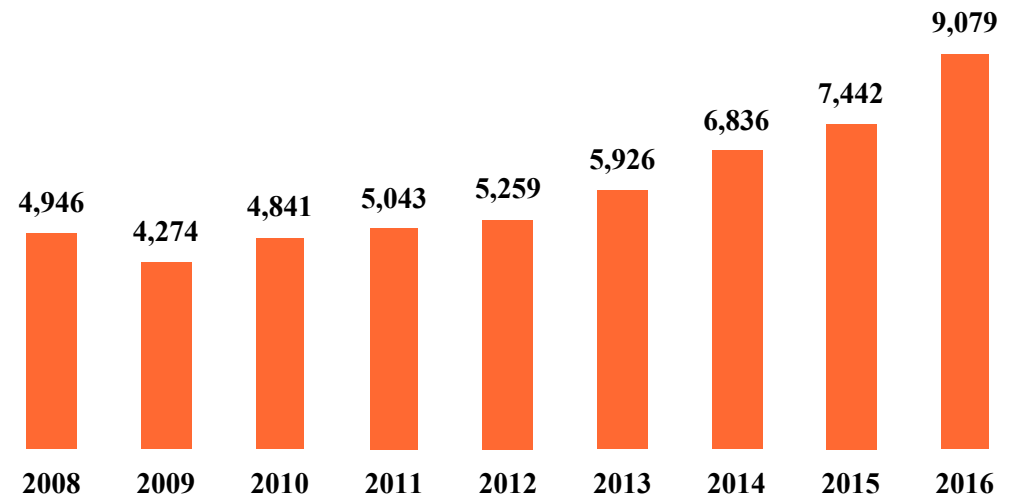
Prevalence

- 15-20 M HDV infected patients worldwide
- 4-6% of HBV infected patients

Increased HDV Patient Diagnosis

~110,000 Individuals Co-infected with HBV/HDV in U.S.

Newly Diagnosed Patients by ICD-10

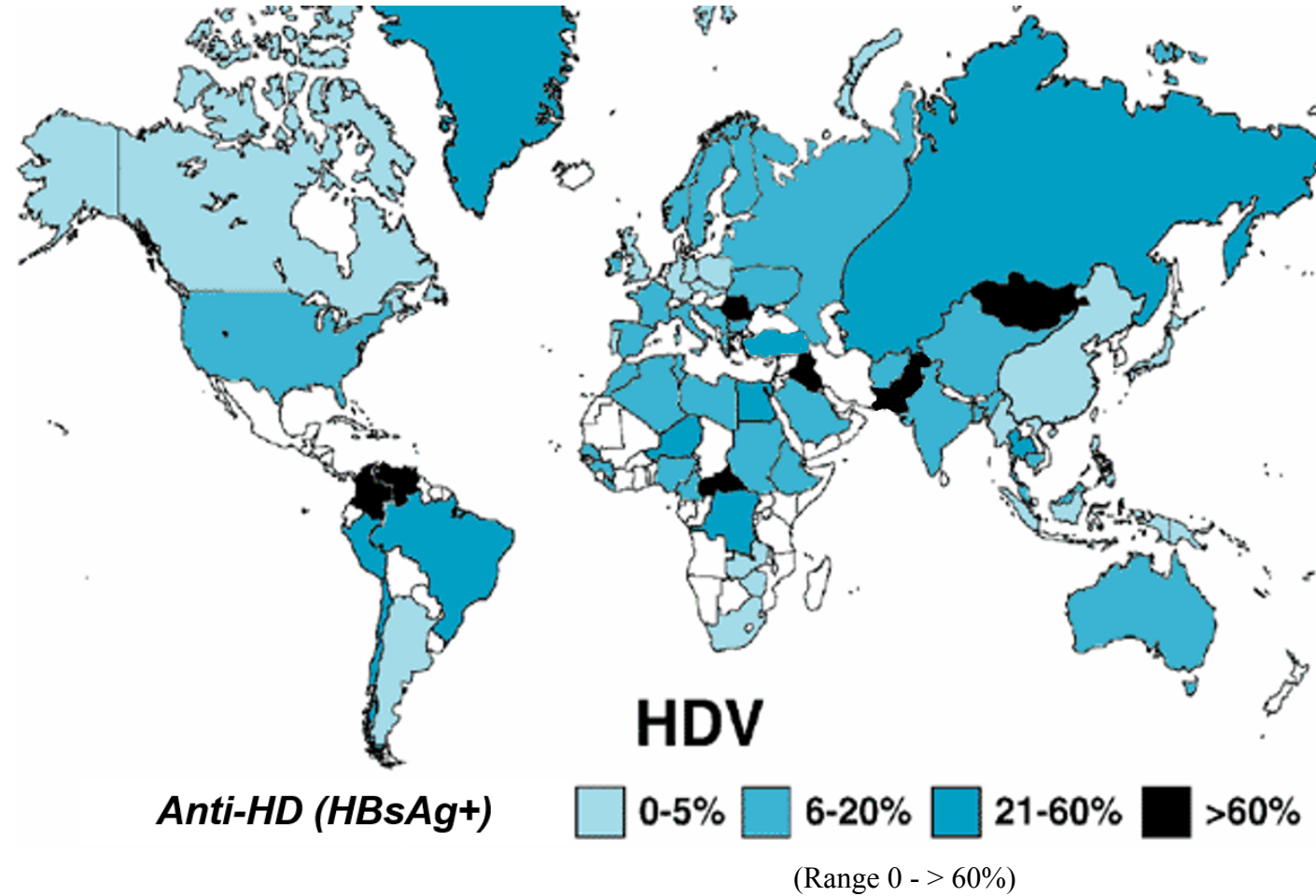


Lonafarnib Phase 2
Data Presentations



HDV WORLDWIDE PREVALENCE: 15-20 MILLION

6% of HBV Population Infected with HDV



MIGRATION AND VIRAL HEPATITIS

Globalization of Disease

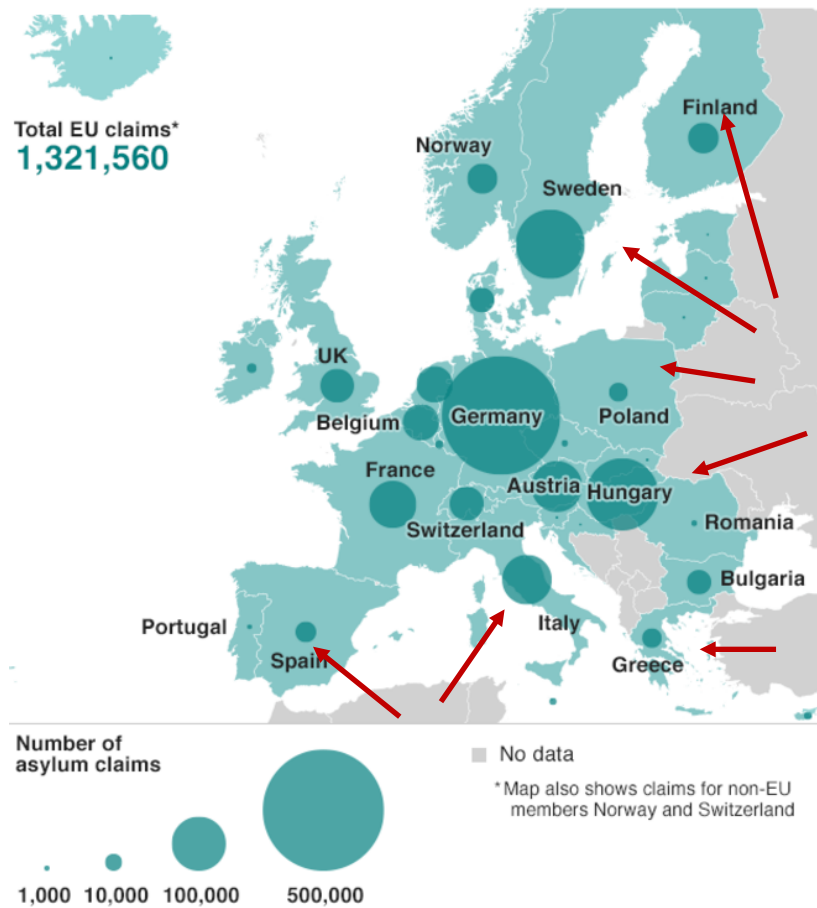


Foreign-born individuals comprise majority of growing HDV positive population in North America and Western Europe...

Germany:	Wedemeyer et al., Hepatology 2007 Heidrich et al., J Viral Hepatitis 2009
France:	Le Gal et al., Hepatology 2007
UK:	Cross et al., J Med Virol 2008
Italy:	Stroffolini et al., J Med Virol 2009 Piccolo et al., Eur J Publ Health 2010

MIGRATION INTO WESTERN EUROPE

Known Claims for Asylum in 2015 > 1 Million



Source: Eurostat

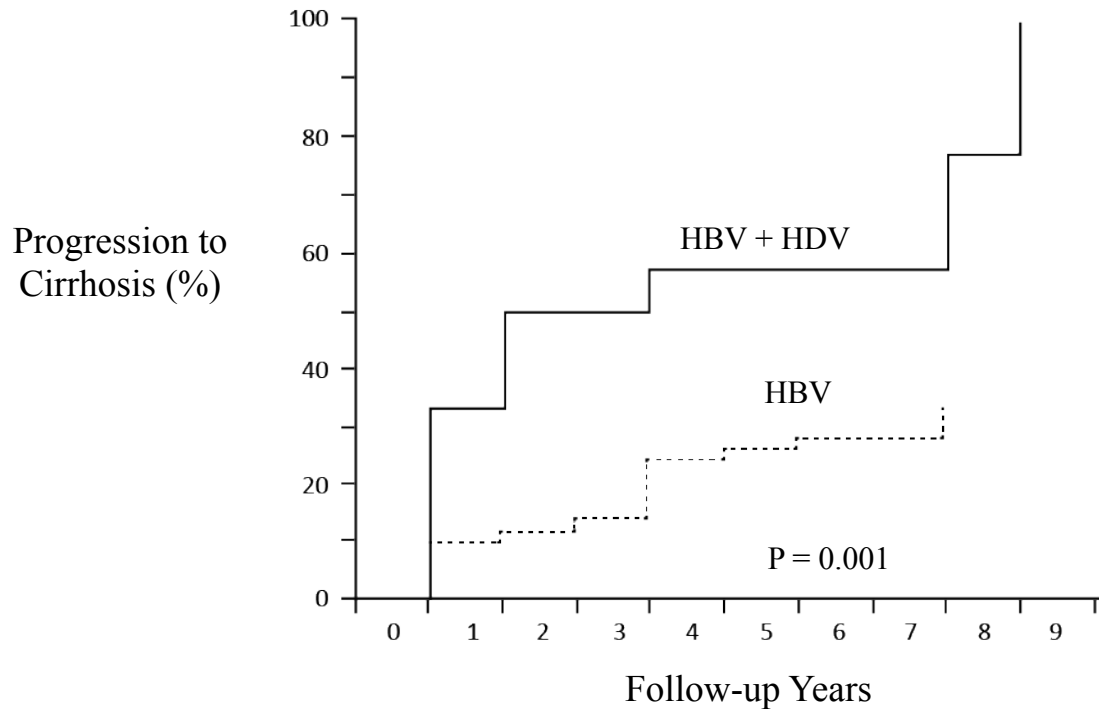
BBC



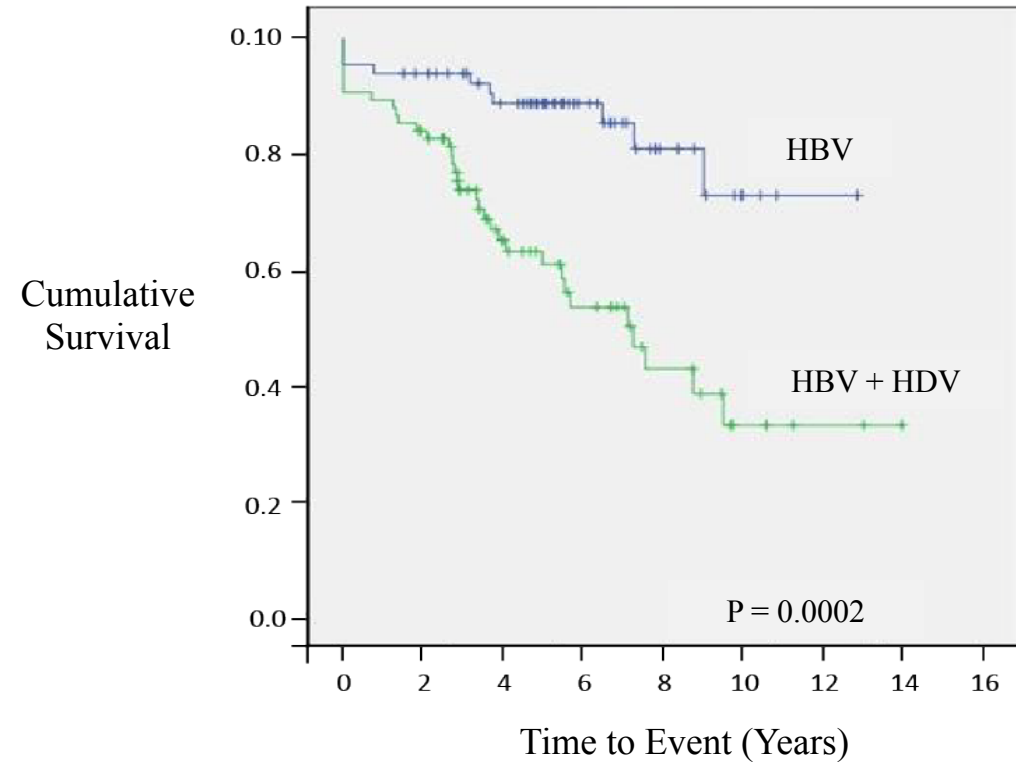
AT DIAGNOSIS, >50% OF HDV PATIENTS ARE CIRRHOTIC

Risk of Hepatocellular Carcinoma, Decompensation, Mortality Increase

Evolution from Chronic Active Hepatitis to Cirrhosis

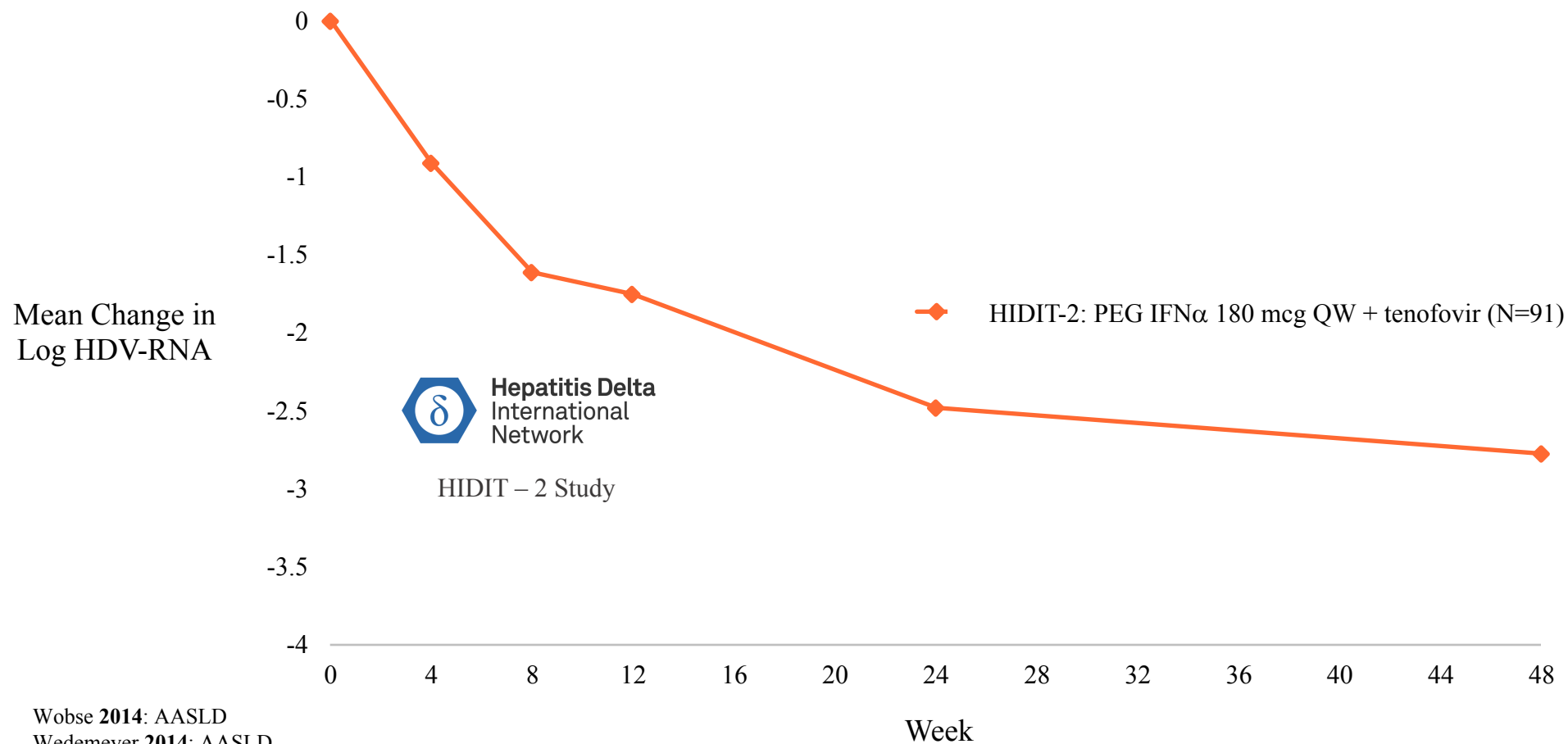


Survival



PEG IFN- α HAS MODEST BENEFIT IN HDV

Tolerability a Problem, Rebound a Problem, Retreatment a Problem



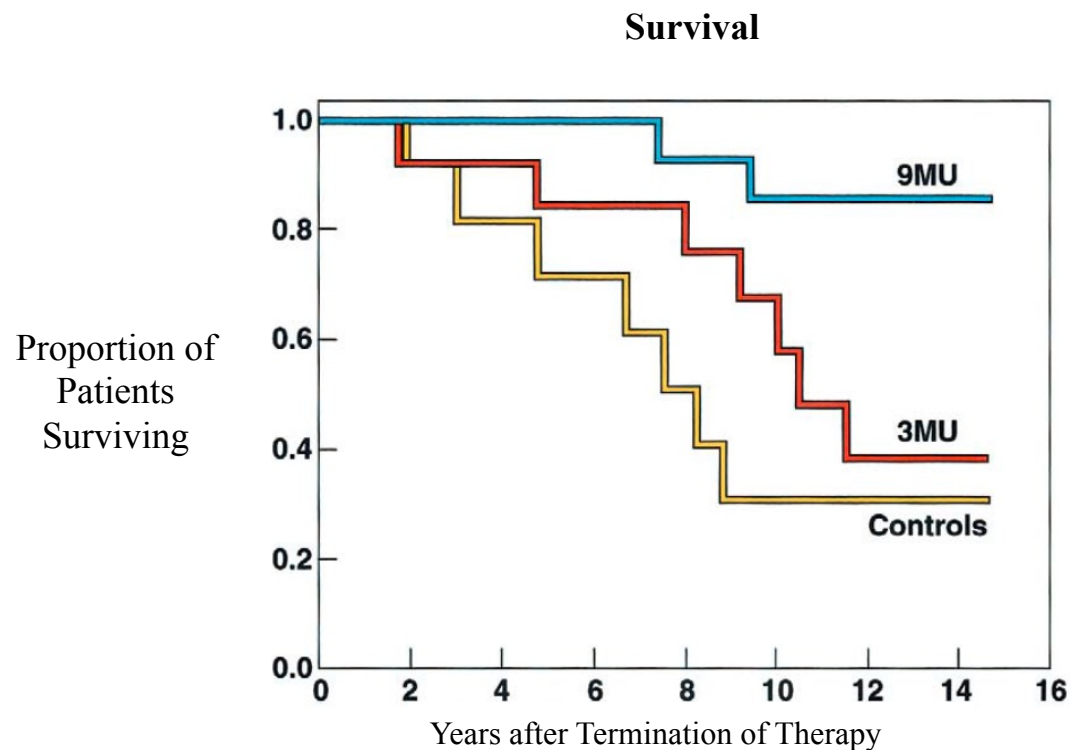
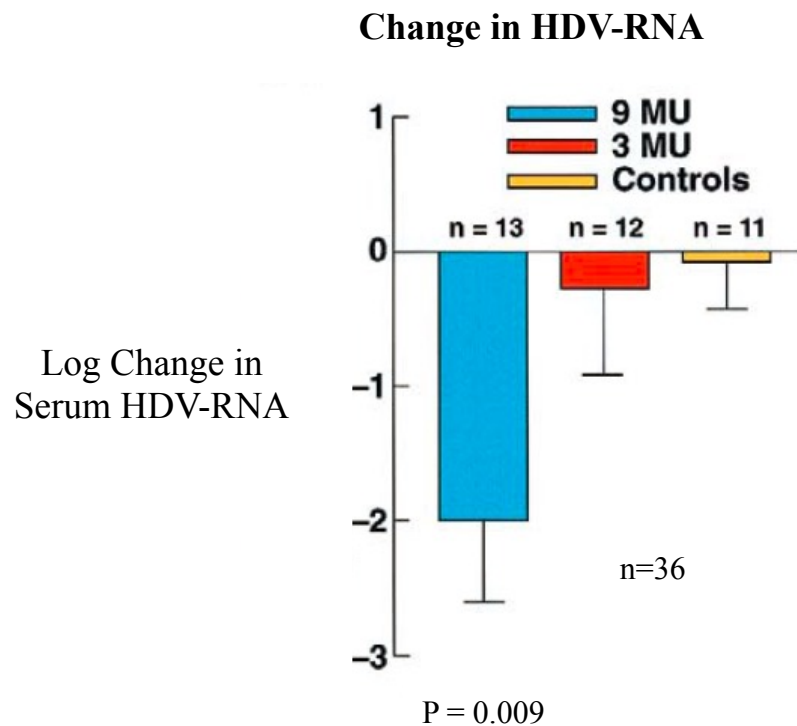
**-2.5 log mean reduction
in HDV-RNA at 48 weeks**

SVR rates ~ 25-30%

REDUCING HDV-RNA IMPROVES SURVIVAL

Improved Clinical Benefit without Clearance of HDV-RNA

Interferon- α for 48 weeks with 15 year Follow Up

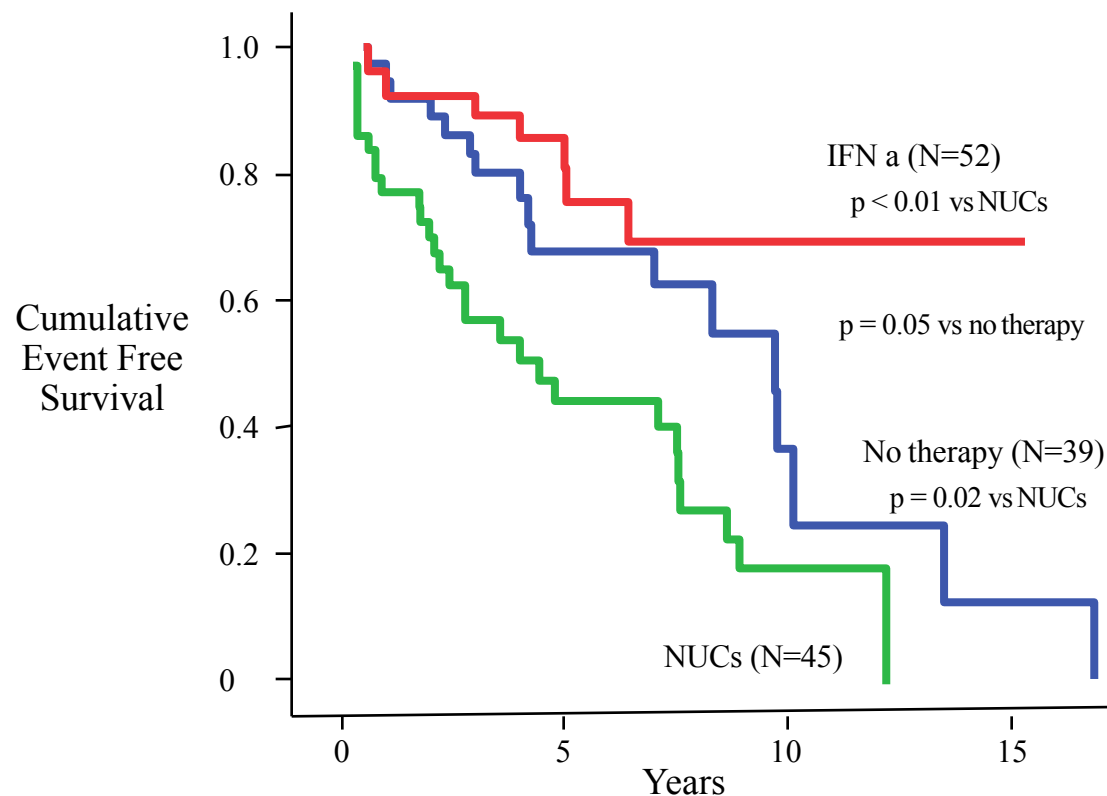


FEWER CLINICAL EVENTS FOLLOWING IFN α

HDV-RNA Loss Improves Long-term Clinical Outcomes

Interferon- α for 48 weeks with up to 18.8 Year Follow Up

- Long term clinical outcomes
 - IFN alfa treatment in HDV
- Retrospective analysis
 - single cohort study
- 136 anti-HDV positive patients
- Median follow-up: 5.2 years
 - Range 0.6 -18.8 years



WHAT ENDPOINTS HAVE BEEN USED IN HDV?

PROPOSED ENDPOINTS IN HDV

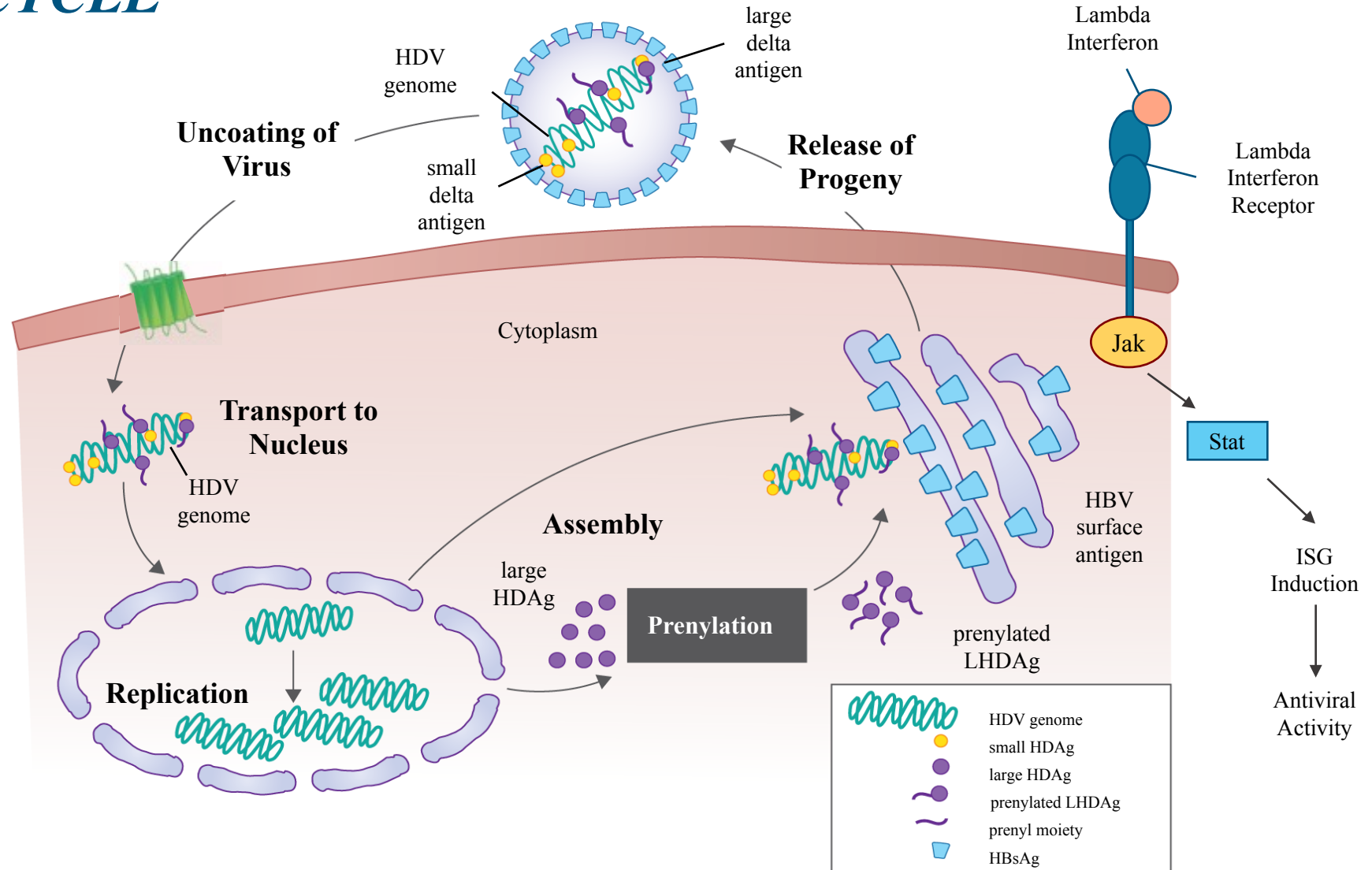
- Primary Endpoint: Reduction in HDV RNA
 - ≥ 2 Log Reduction in HDV RNA at EOT
- Secondary Endpoint: Biopsy Confirmed Histologic Improvement
 - 2 point improvement in HAI inflammation score without progression in Fibrosis at EOT
 - ALT Normalization at EOT



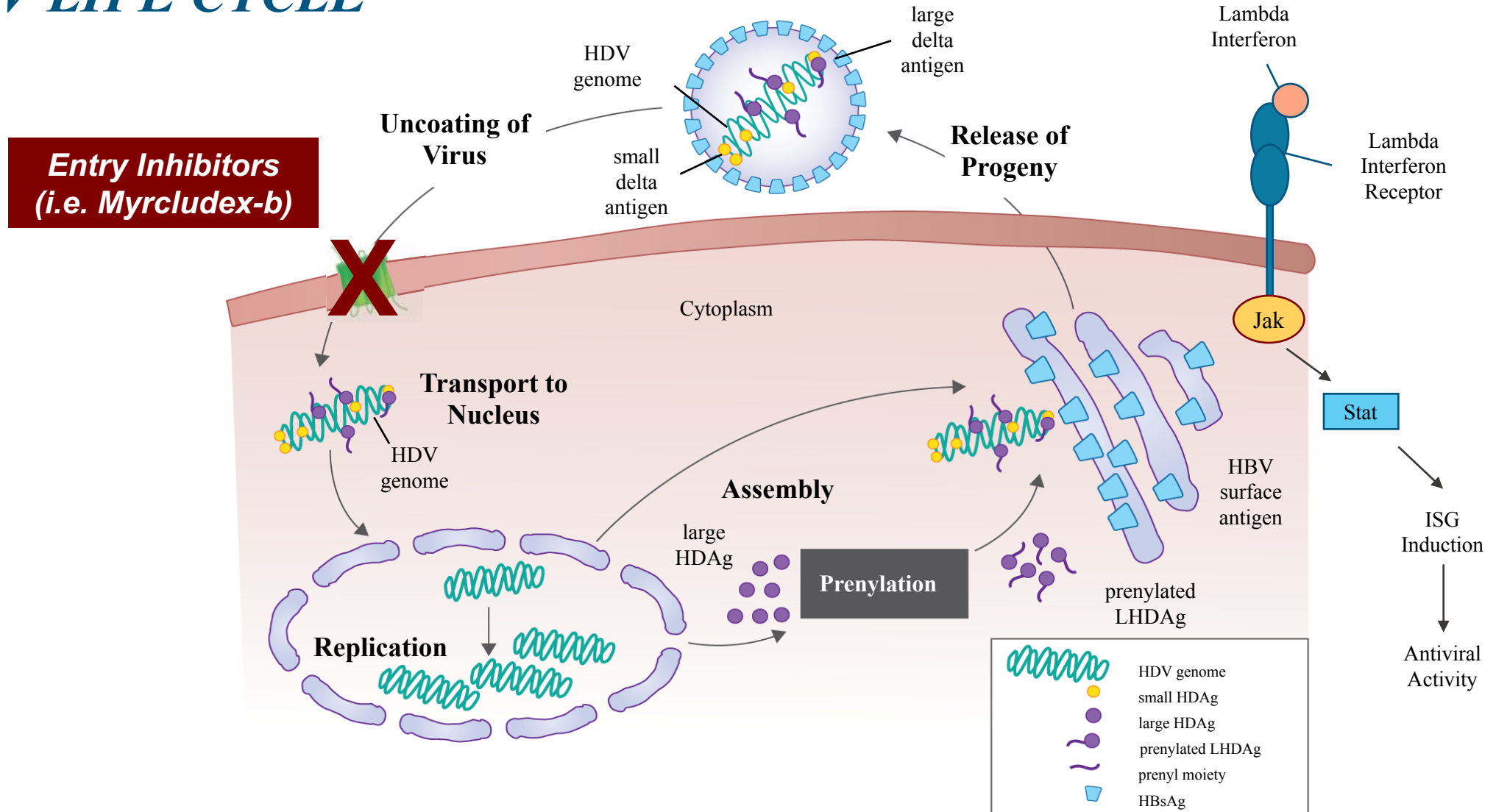
White Paper to be submitted by
Hepatitis Delta International Network
(HDIN) in October



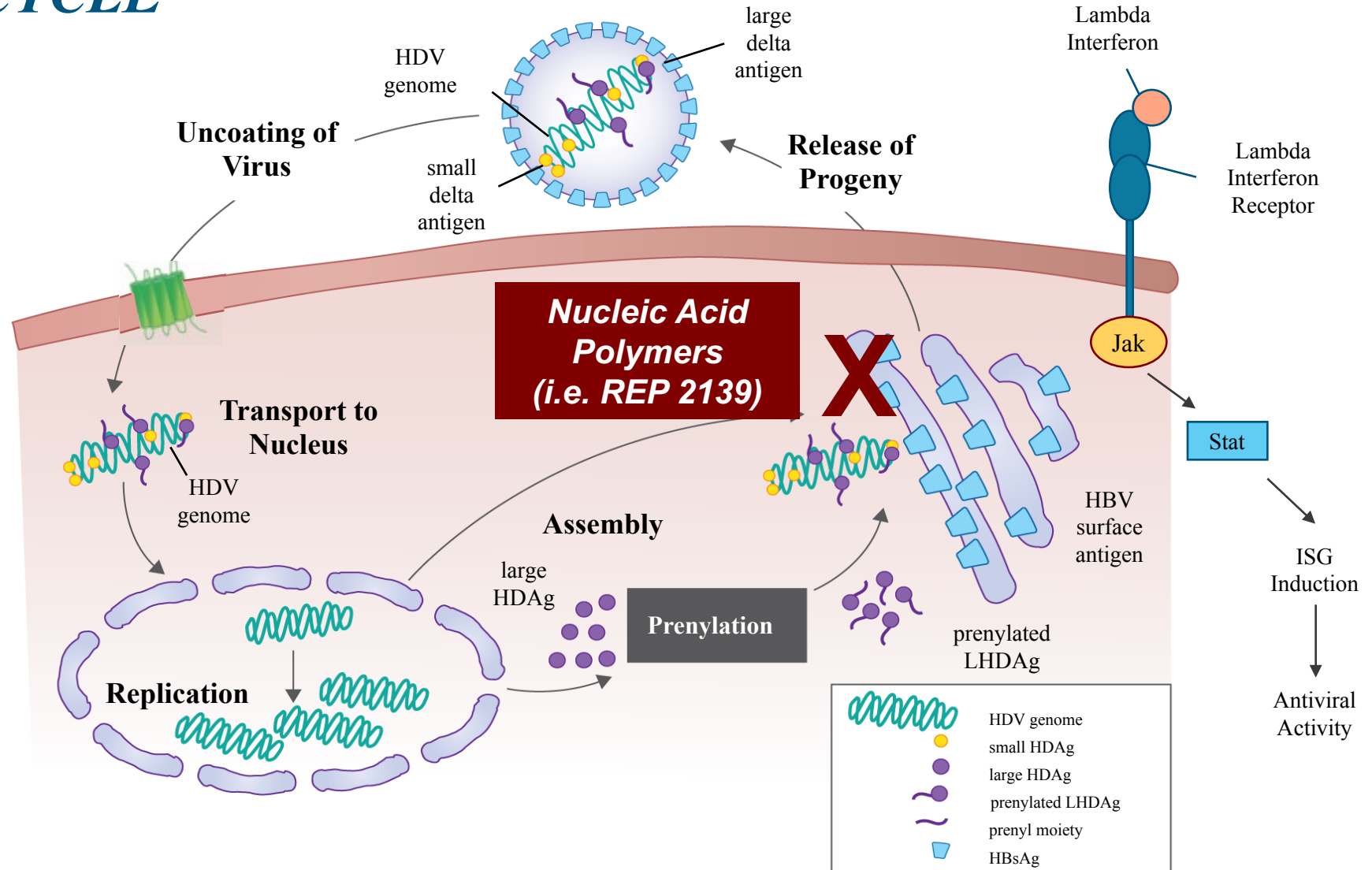
HDV LIFE CYCLE



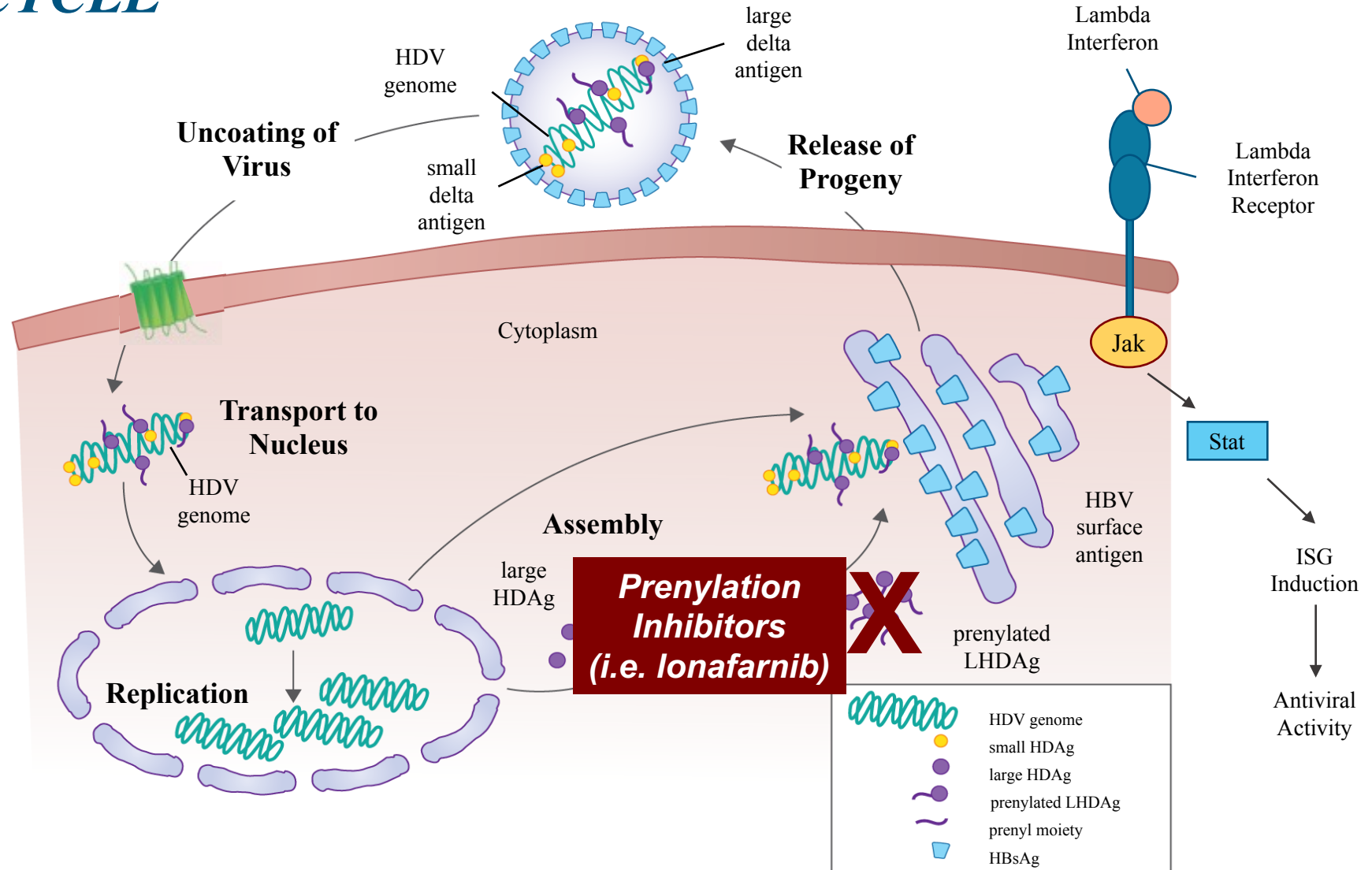
HDV LIFE CYCLE



HDV LIFE CYCLE



HDV LIFE CYCLE



HDV LIFE CYCLE

