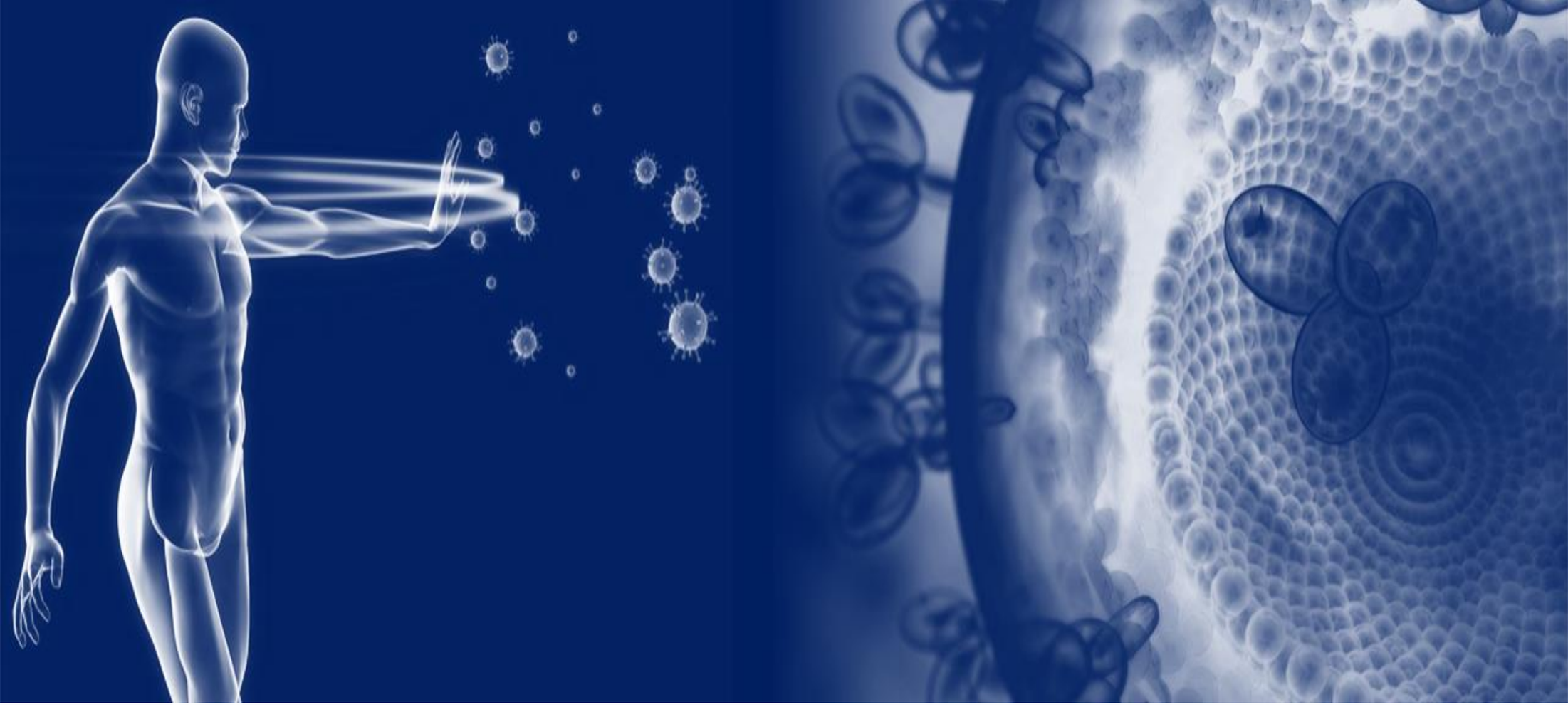

Clinical update, antiviral effect and mode of action of capsid assembly modulators

MAKE HEPATITIS HISTORY

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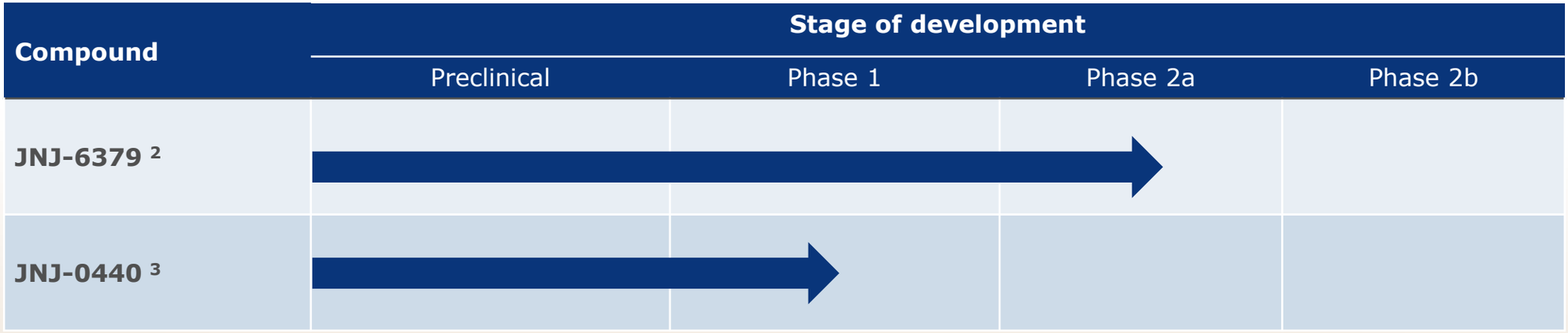
Janssen in Hepatitis B
New Directions Towards a Functional Cure

- Hepatitis B is a major global health problem: an estimated 292 million people are living with chronic HBV infection[1]
- Current HBV treatments do not adequately fulfil the requirements for either a HBV functional or complete cure; consequently, infection remains for life, increasing the risk of liver disease
- Janssen's vision and ongoing efforts are to identify and advance additional direct-acting antivirals and immune-based agents in a pursuit of transforming current treatments by offering a novel, finite, functional cure for HBV
- Janssen has hepatitis B direct-acting antivirals and immune modulators at various stages of early clinical development including the two capsid assembly modulators (CAMs) JNJ-56136379 (JNJ-6379) and the more potent JNJ-64530440 (JNJ-0440)



[1] The Polaris Observatory Collaborators. Lancet Gastroenterol Hepatol. 2018;3:383-403
[2] ClinicalTrials.gov Identifier: NCT02662712 and NCT03361956
[3] ClinicalTrials.gov Identifier: NCT03439488

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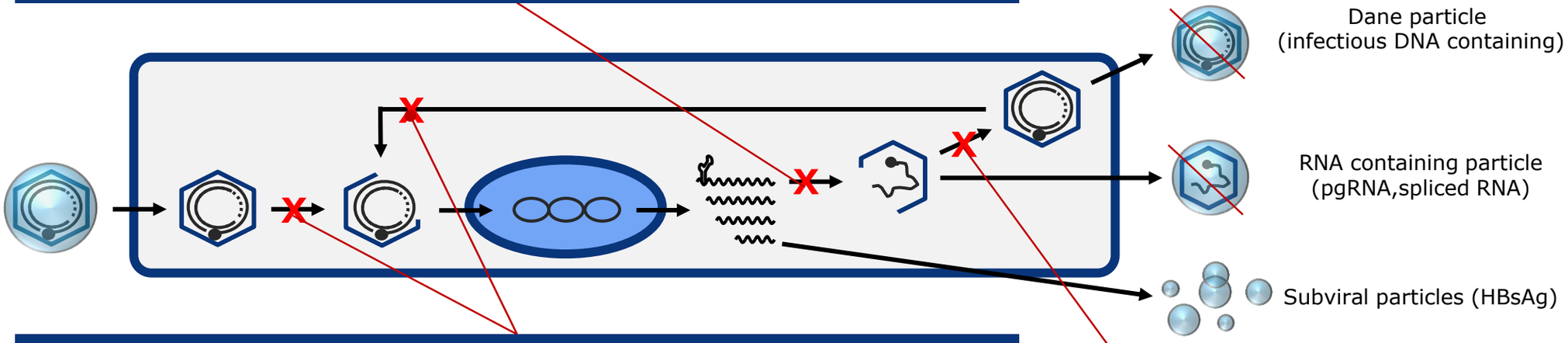
CAMs with a dual mechanism of action

JNJ-6379 and JNJ-0440 bind to HBV core protein and disrupt early and late-stage processes in the HBV life cycle.

"Primary" mechanism
Interference with capsid assembly kinetics, preventing encapsidation of (pg)RNA and blocking HBV replication (late step in viral life cycle)



"Secondary" mechanism
Inhibition of the de-novo formation of cccDNA, potentially by interfering with the capsid disassembly process (early step in viral life cycle)

NAs block replication but do not inhibit the production of RNA-containing particles

Triggering of the secondary mechanism occurs at a much higher concentration than for the primary mechanism.

PHH Primary Human Hepatocytes
Berke JM et al. AASLD 2016; Abstract 234

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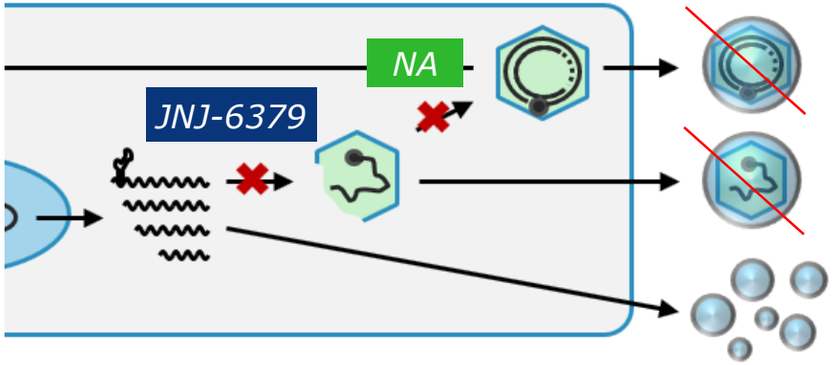
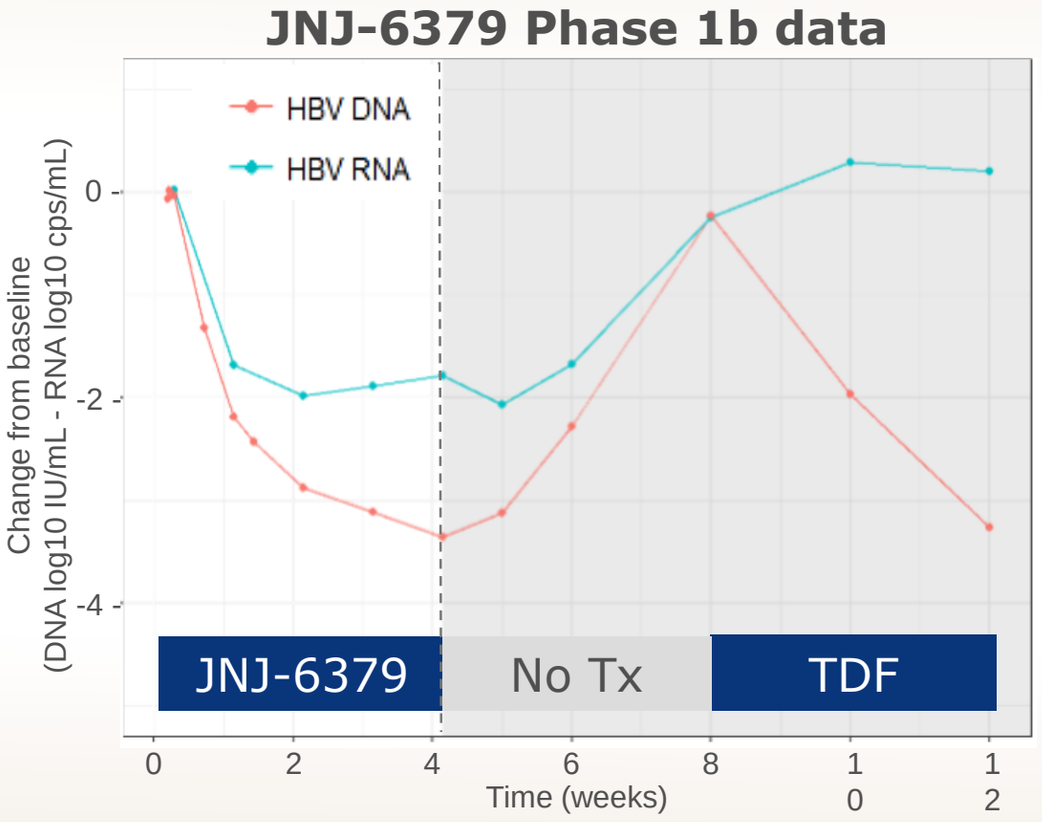
JNJ-6379 inhibits production of HBV DNA and RNA containing particles

"Primary" mechanism - late step in viral life cycle



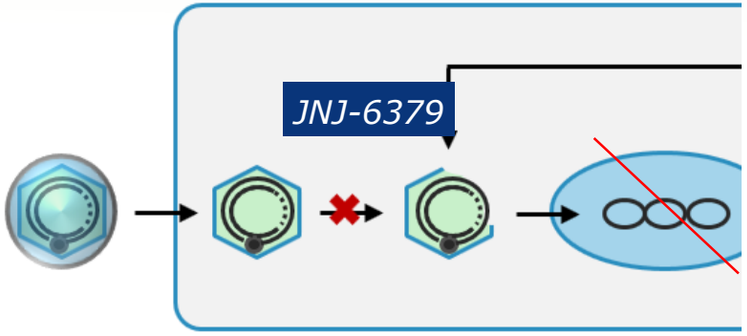
Nucleos(t)ides analogs do not inhibit the production of RNA containing particles



Tx = treatment
TDF = tenofovir disoproxil fumarate
Berke JM. Discovery on Target Workshop 2018; keynote presentation

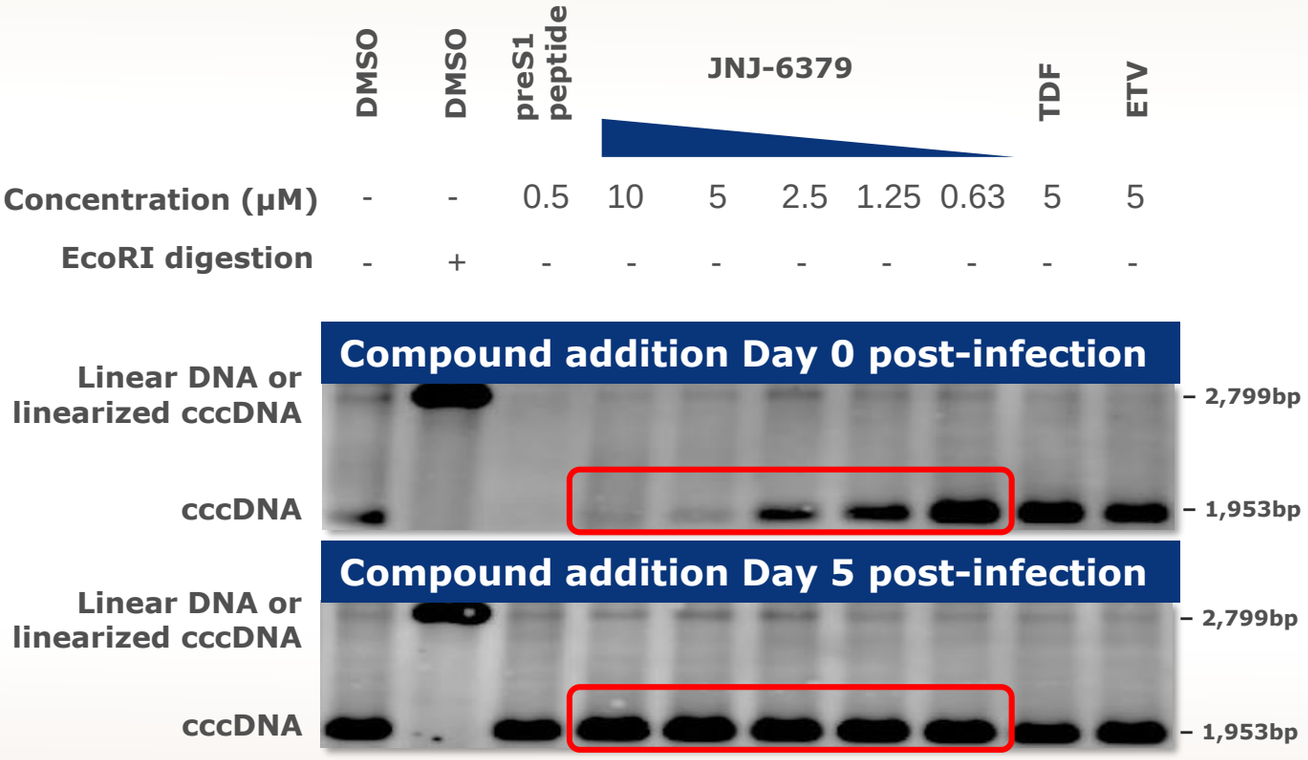
JNJ-6379 inhibits cccDNA formation in HBV-infected PHH

"Secondary" mechanism - early step in viral life cycle



Dose-dependent inhibition of cccDNA formation in presence of JNJ-6379 when added together with viral inoculum

No inhibition of cccDNA formation observed with nucleos(t)ide analogs



PHH = Primary human hepatocytes
Berke, JM *et al.* AASLD 2016

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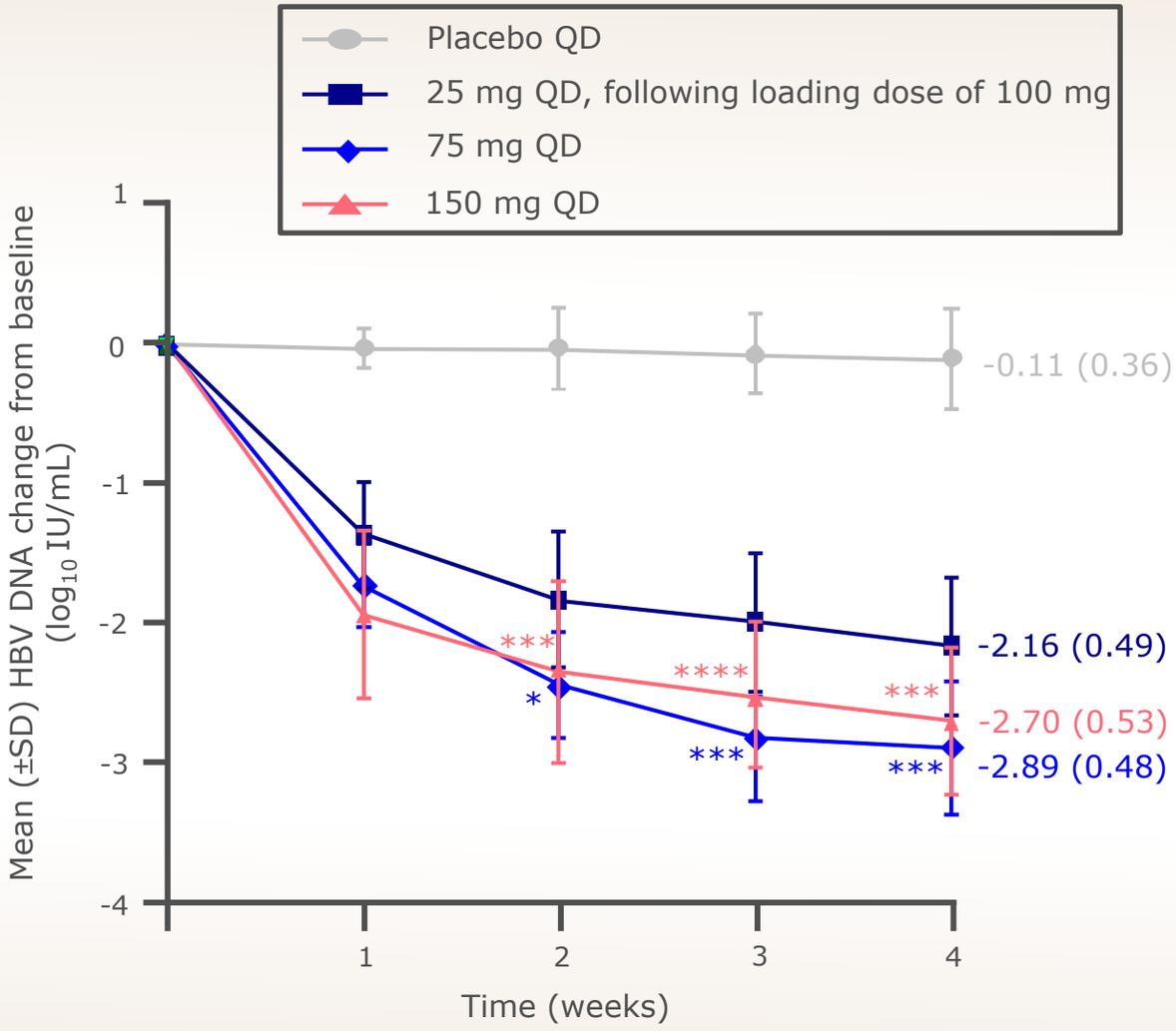
Mean HBV DNA change from baseline

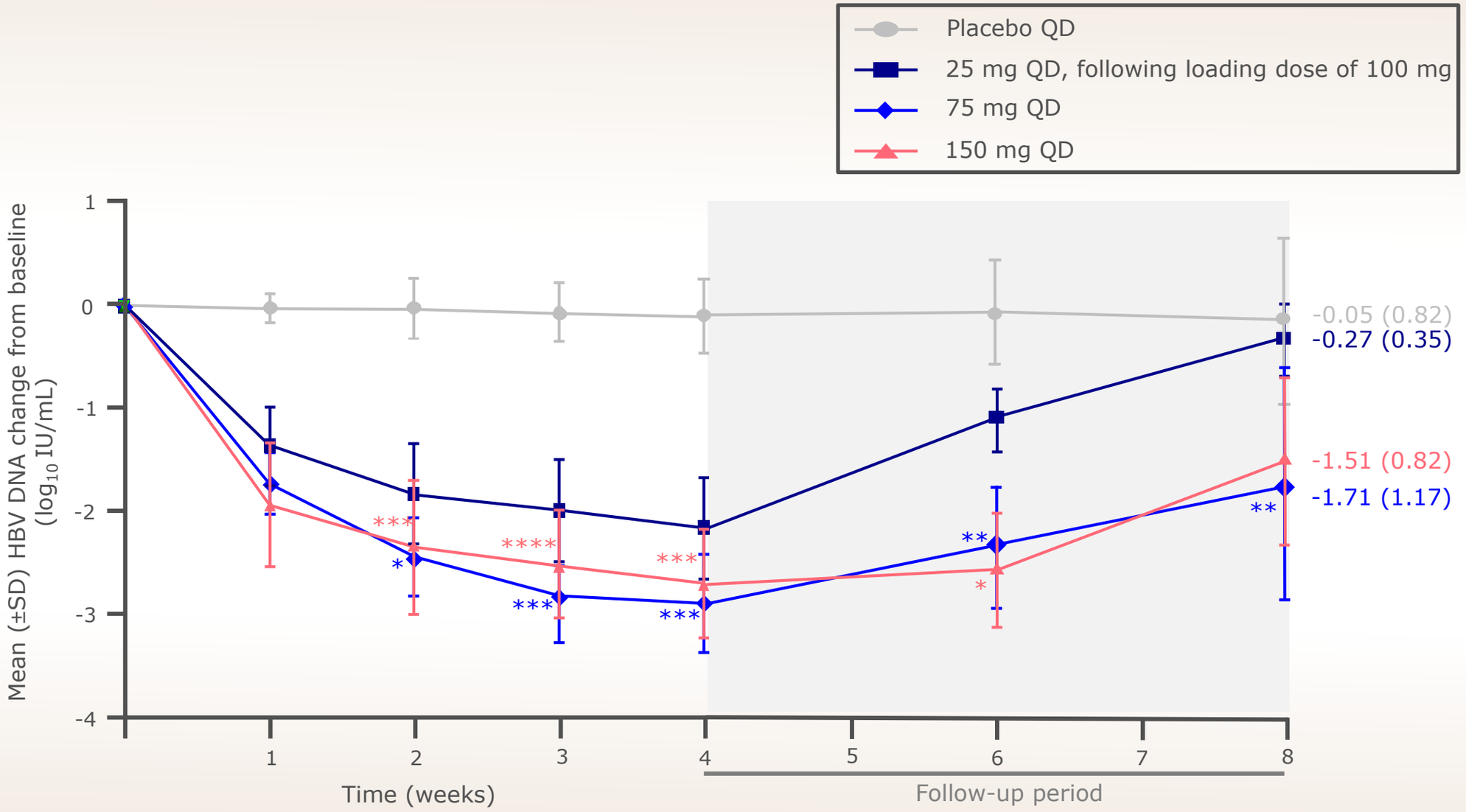
HBV DNA				
	Baseline		Day 29	
Dose group	N	Mean (SD) log_{10} IU/mL	Mean (SD) Change from Baseline log_{10} IU/mL	<LLOQ n (%)
JNJ-6379 25 mg	8	6.90 (1.91)	−2.16 (0.49)	0
JNJ-6379 75 mg	8	5.26 (1.50)	−2.89 (0.48)	3 (38%)
JNJ-6379 150 mg	9	5.10 (1.56)	-2.70 (0.53)[a]	3 (38%)[a]
Pooled placebo	11	5.10 (1.64)	-0.04 (0.28)	0

[a] HBV DNA at Day 29 is available for 8 patients



Each * refers to one patient with HBV DNA <lower limit of quantification of the HBV DNA assay

Mean HBV DNA change from baseline



Each * refers to one patient with HBV DNA <lower limit of quantification of the HBV DNA assay

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Mean HBV DNA and HBV RNA change from baseline after 4 weeks on treatment

	HBV RNA			
	Baseline[a]		Day 29	
Dosing group	N	Mean (SD) log_{10} cp/mL	Mean (SD) Change from Baseline log_{10} cp/mL	Not detected n (%)
JNJ-6379 25 mg QD	8	5.59 (2.37)	−2.30 (0.59)	3 (38%)
JNJ-6379 75 mg QD	8	3.39 (2.21)	−1.85 (1.42)	6 (75%)
JNJ-6379 150 mg QD	9	3.37 (1.66)	-1.83 (0.93)[b]	6 (75%)[b]
Pooled placebo	11	3.33 (2.58)	0.02 (0.86)	3 (27%)

[a] Two patients in the 75 mg JNJ-379 group, one patient in the 150 mg JNJ-6379 group and three patients in the placebo group had undetectable HBV RNA at baseline

[b] HBV RNA at Day 29 is available for 8 patients

LLOQ: Lower limit of quantification

No relevant changes in HBsAg or HBeAg were observed

Zoulim F et al, EASL, Paris, 14 April 2018, oral presentation

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Summary

- As part of a mixed portfolio of hepatitis B direct-acting antivirals and immune modulators, Janssen has two capsid assembly modulators (CAMs) in early clinical development

JNJ-6379

- JNJ-6379 administered orally for 28 days at doses of 25 mg, 75 mg or 150 mg QD demonstrated potent antiviral activity by reducing HBV DNA and HBV RNA; as anticipated in the four-week period, there were no relevant changes in HBsAg
- All three of these dose regimens were safe and well tolerated, and displayed dose-proportional pharmacokinetics
- A Phase 2a study in treatment-naïve and virologically-suppressed HBeAg positive and negative CHB patients has been initiated to evaluate JNJ-6379 alone or in combination with nucleos(t)ide analogs

JNJ-0440

- JNJ-0440 is a more potent CAM than JNJ-6379 which may translate into superior efficacy in clinical studies
- The safety, tolerability and PK of single and multiple ascending oral doses of JNJ-0440 in healthy adults are being evaluated in a Phase 1, double-blind, randomized, placebo-controlled study
- Single oral doses of JNJ-0440 administered up to 900 mg have been well tolerated in healthy adults

- Updates on the clinical development of JNJ-6379 and JNJ-0440 will be presented this week at AASLD

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Thank you

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