

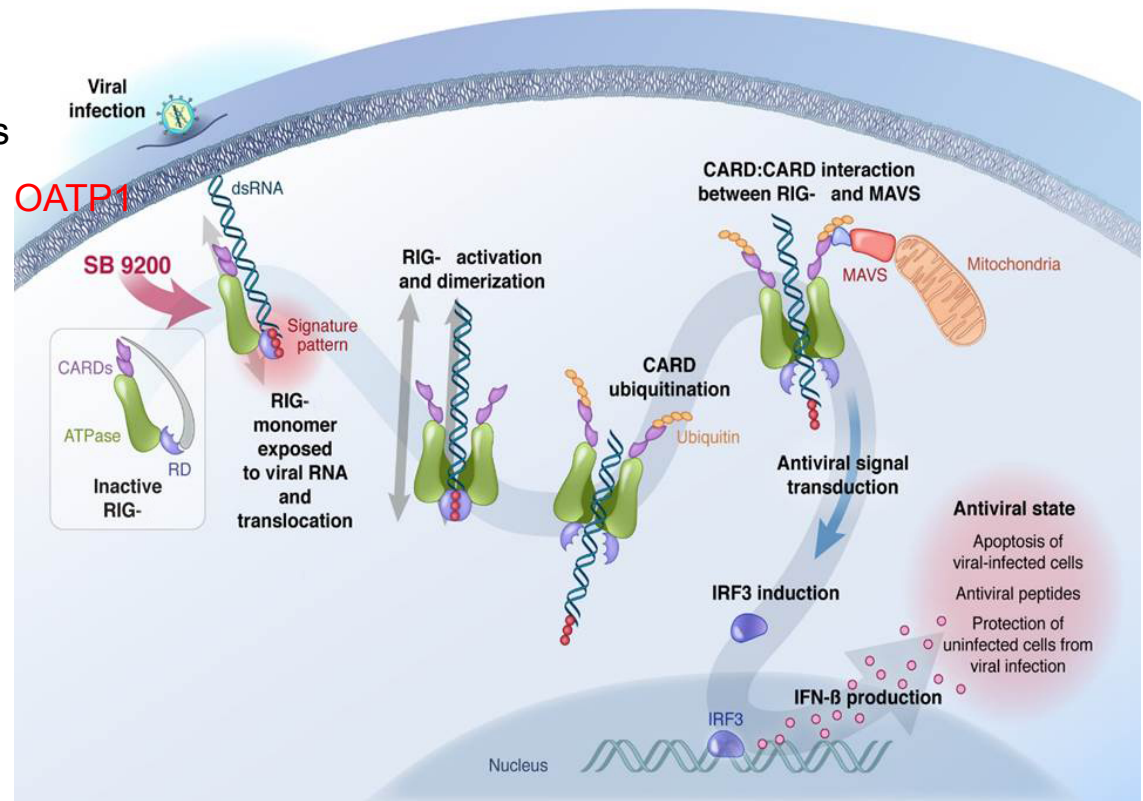
## Forward Looking Statements

Any statements in this presentation about our future expectations, plans and prospects, including statements regarding our strategy, future operations, prospects, plans and objectives, and other statements containing the words "believes," "anticipates," "plans," "expects," "potential," "could," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: whether our cash resources will be sufficient to fund our continuing operations for the period anticipated; whether results obtained in preclinical studies and early clinical trials will be indicative of results obtained in future clinical trials; whether SB 9200 and our other product candidates will advance through the clinical trial process on a timely basis and receive approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies; whether, if SB 9200 or any of our other product candidates obtain approval, it will be successfully distributed and marketed; and other factors discussed in the "Risk Factors" section of our Form 10-Q filed August 1, 2016. In addition, the forward-looking statements included in this presentation represent our views as of September 1, 2016. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so.

# SB 9200 Stimulates Interferon Production and Induces Immune Response

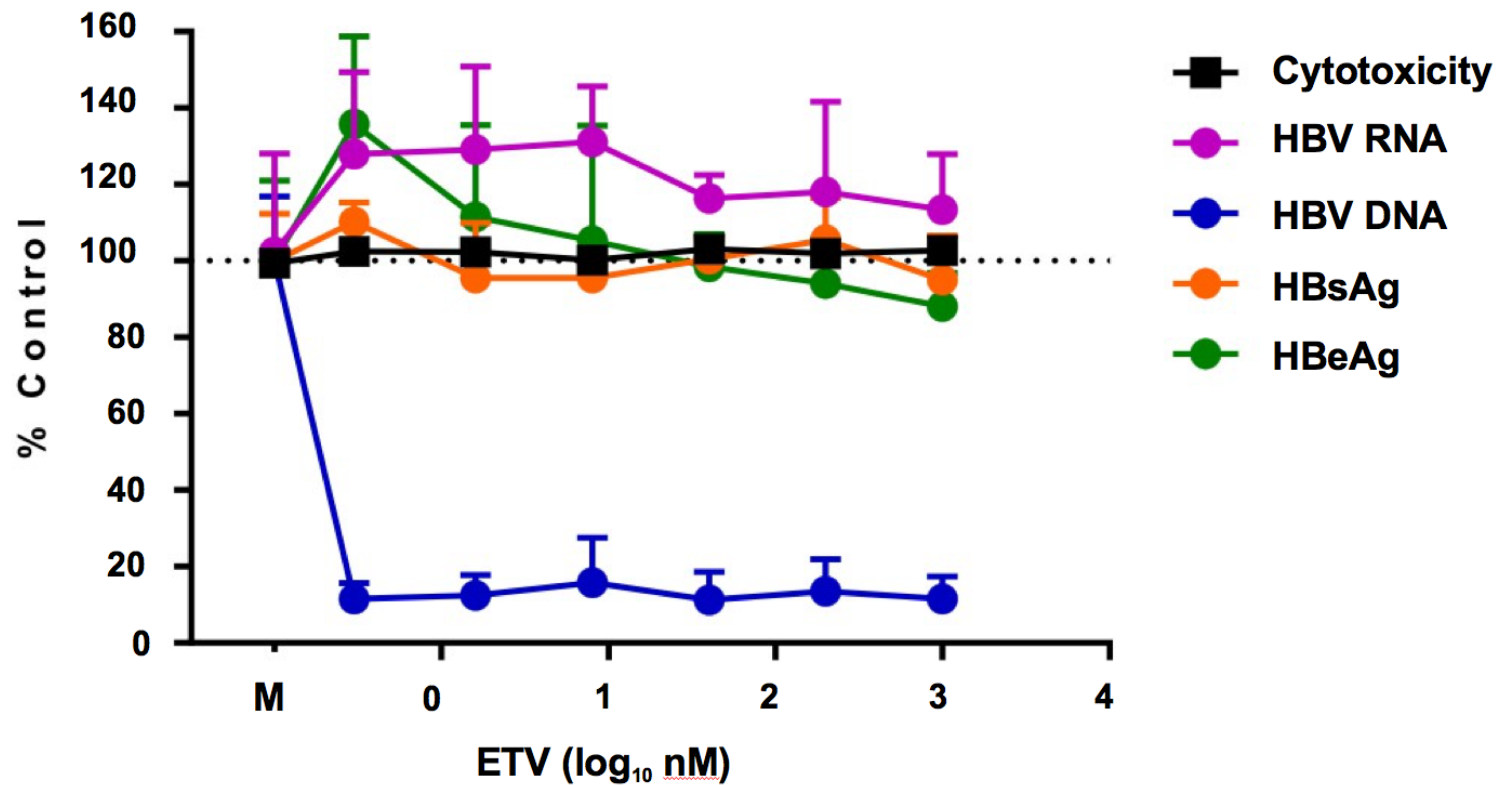
## Key Characteristics

- Binds and activates RIG-I and NOD2 – sentinel proteins in the body's innate defense system
- Only active in cells with virus present
- Launches adaptive immune response
- Synergistic with other drugs and active against resistant strains
- Activates “host” targets instead of viral targets – potential for higher barrier to viral resistance

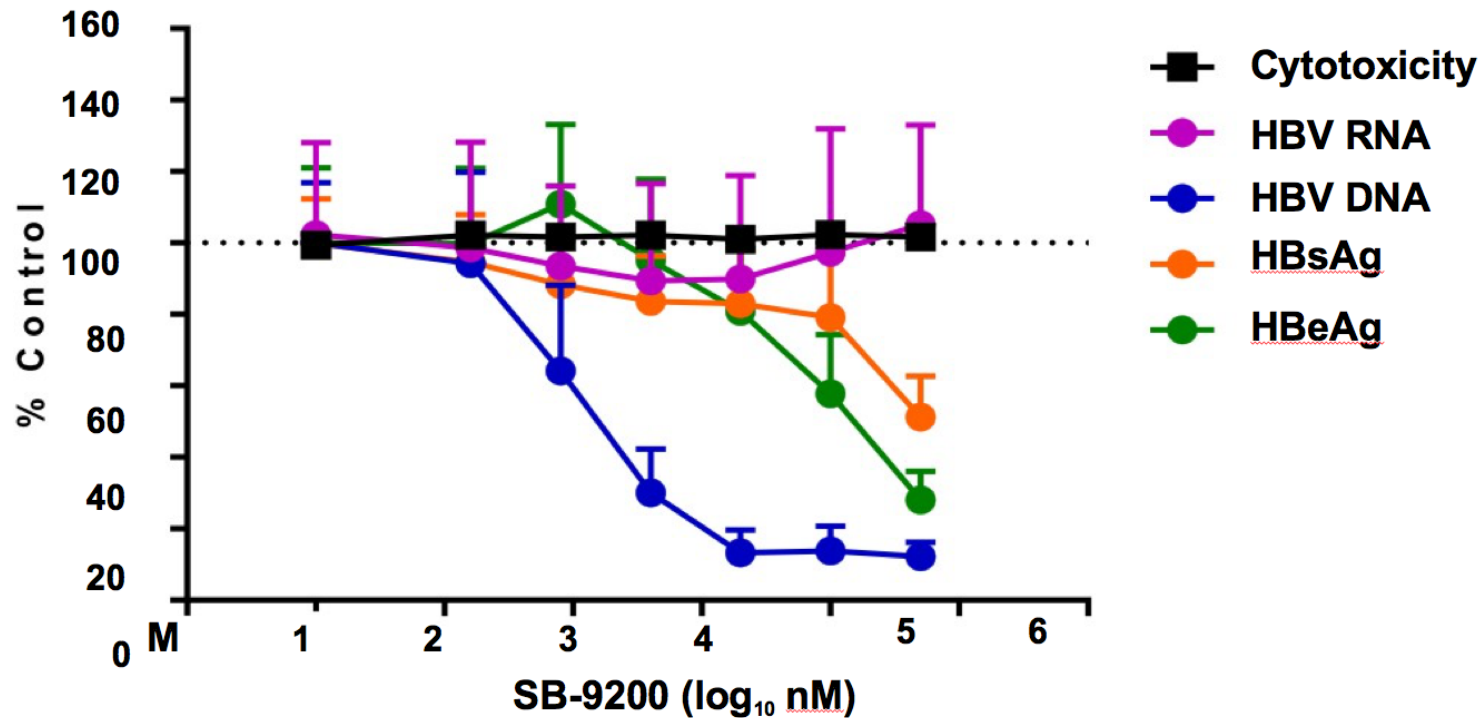


*Evidence suggests host immune response is necessary for viral clearance and functional cure*

# Entecavir, a Potent Inhibitor of HBV DNA, has no Effect on Viral RNA or Viral Antigens



# Dose-dependent Inhibition of Viral DNA, HBsAg and HBeAg by SB 9200



# *In vivo* HBV Studies Support Clinical Development of SB 9200

## Woodchuck hepatitis virus (WHV) and its host, the American woodchuck, is accepted by KOLs, as the most predictive animal model for human HBV infection

- Similarities in morphology, genome structure, gene products, replication, and epidemiology were noted
- Also useful as a model for PK/PD and assessment of drug toxicity

### Study Design

- **Study 1:** SB 9200 at 15 mg/kg/day or 30 mg/kg/day for 12 weeks
- **Study 2:** SB 9200 at 30 mg/kg/day for 12 weeks followed by four weeks of entecavir (ETV) at 0.5 mg/kg/day
- Serum WHV DNA and woodchuck surface antigen (WHsAg) levels, as well as cccDNA, viral RNA, and replication intermediates were assessed

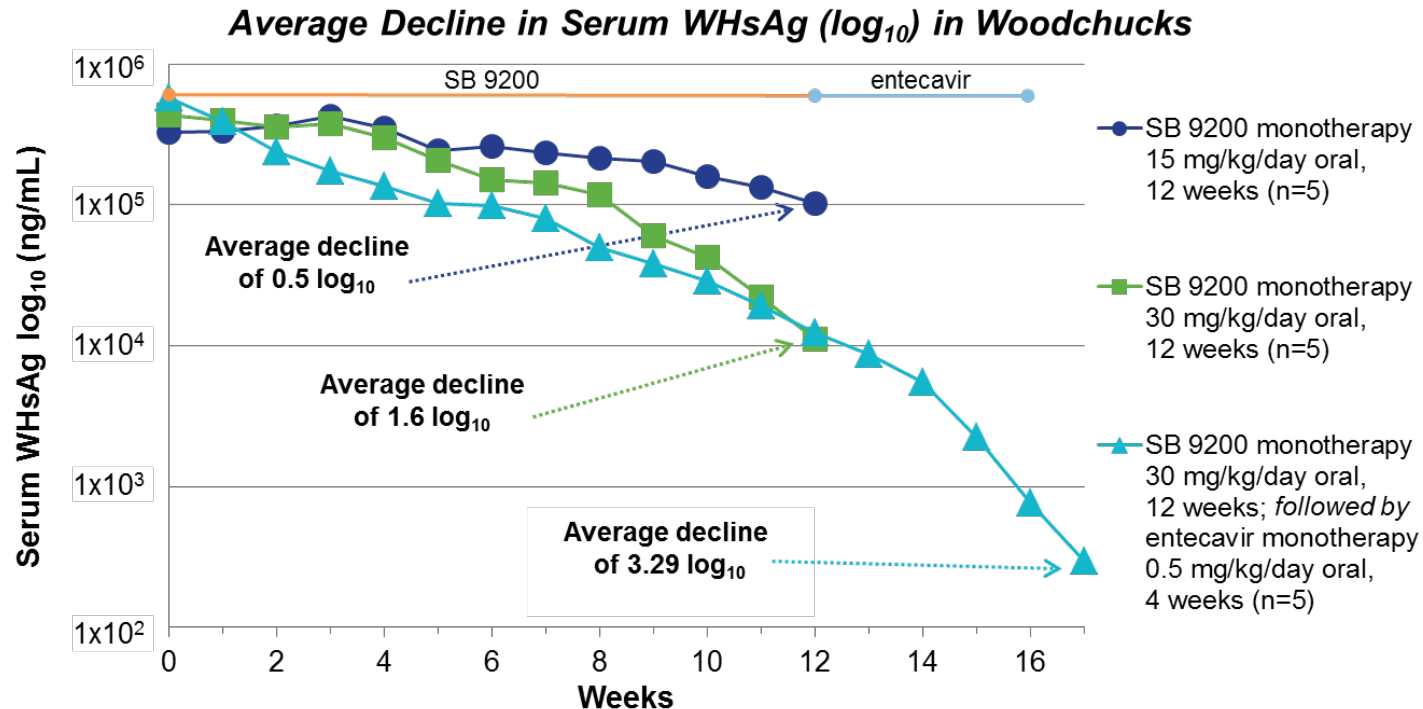
### Study Results

- All animals dosed with SB 9200 showed a treatment response
- SB 9200 demonstrated a dose-dependent reduction in viral DNA and WHsAg in Study 1
- Reductions in cccDNA, viral RNA and replication intermediates were observed
- SB 9200 was well tolerated in both studies with no adverse events observed

# Treatment with SB 9200 Resulted in a Meaningful Decline in Serum WHsAg Levels in Chronically WHV-Infected Woodchucks<sup>(1)</sup>

*Reduction of serum WHsAg in sequential dosing study believed to support thesis to combine SB 9200 with oral antiviral agents*

ADD ENTER

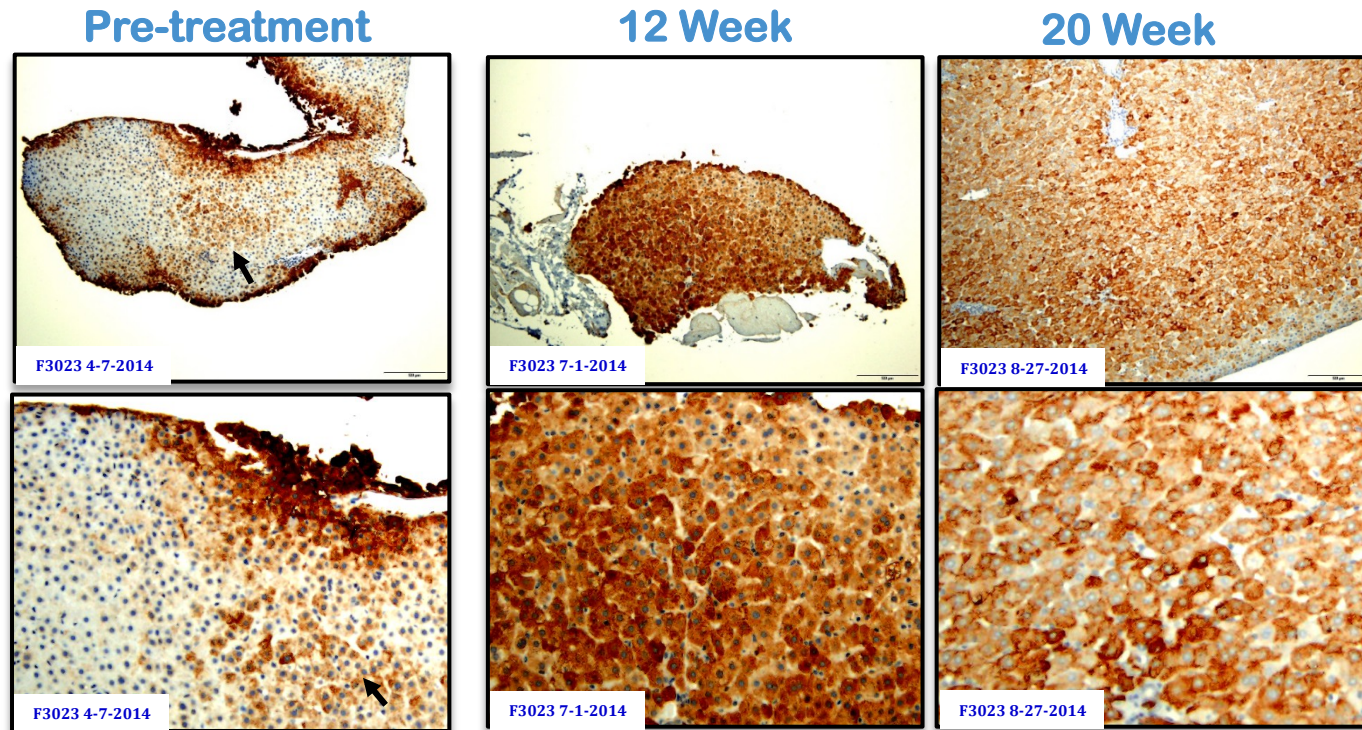


- **Four of five** woodchucks in the sequential dosing study of SB 9200 and entecavir demonstrated serum WHsAg levels near the lower limit of quantification (LLOQ, 3 at week 17 and 1 at week 20)
- Same third party study evaluating recombinant IFN- $\alpha$  in woodchucks reported an average decline in serum WHsAg of approximately 2.0  $\log_{10}$  following 15 weeks of treatment<sup>(2)</sup>

(1) In collaboration with Dr. Stephan Menne, Georgetown University, and with support from NIH.

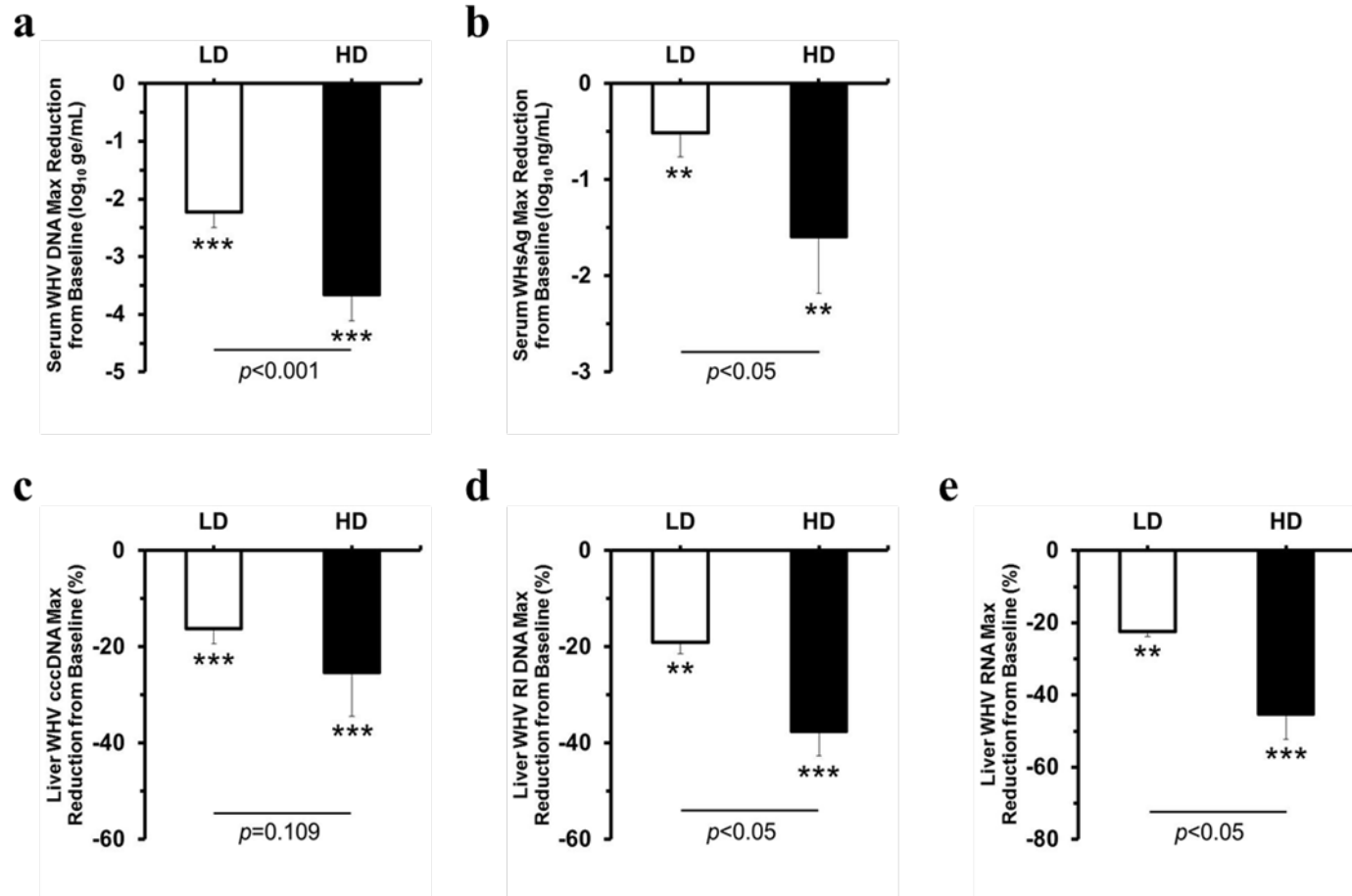
(2) Fletcher SP, Menne S (2015) Intrahepatic Transcriptional Signature Associated with Response to Interferon- $\alpha$  Treatment in the Woodchuck Model of Chronic Hepatitis B. PLOS Pathogens (Sept. 2015).

# Strong Induction of RIG-I by SB 9200 in Virus-infected Woodchucks



Induction of RIG-I supports the antiviral activity of SB 9200 and validates the MOA of SB 9200

# SB 9200 treatment of WHV-infected woodchucks results in significant declines in serum DNA and sAg, and hepatic cccDNA, viral RI DNA and RNA





# SB 9200 – Phase 1 Proof-of-Principle Study in HCV Patients

*Oral bioavailability, safety and antiviral activity in the treatment of HCV patients observed*

## **Phase 1 study in treatment naïve HCV patients**

- Part A: Single ascending doses of 100 – 800 mg, N=8
- Part B: Multiple ascending doses 200 – 900 mg once a day for 7 days, N=30
  - Included both Genotype 1 and 3 patients

## **Dosing up to 900 mg once a day for 7 days was well tolerated**

- No dose limiting toxicities
- No systemic interferon-like symptoms reported
- No nonspecific immune response observed
- No SAEs attributed to SB 9200

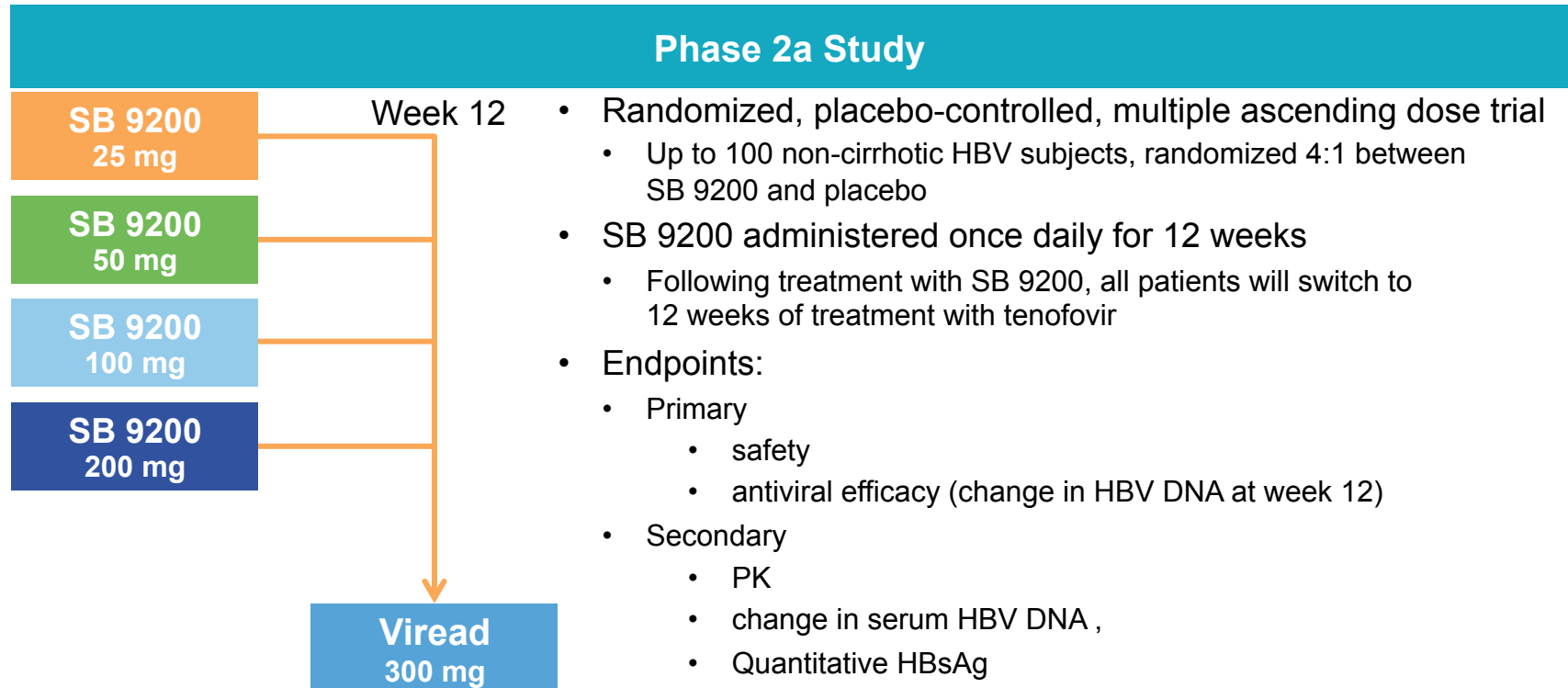
## **Biomarker data affirmed novel mechanism of action (MOA)**

- Induction of intracellular interferon signaling pathways demonstrated
- Antiviral activity was observed at all dose levels

*Study demonstrated proof-of-principle for SB 9200 as a host immunomodulator*

# Phase 2 ACHIEVE Clinical Study of SB 9200 in HBV – Part A

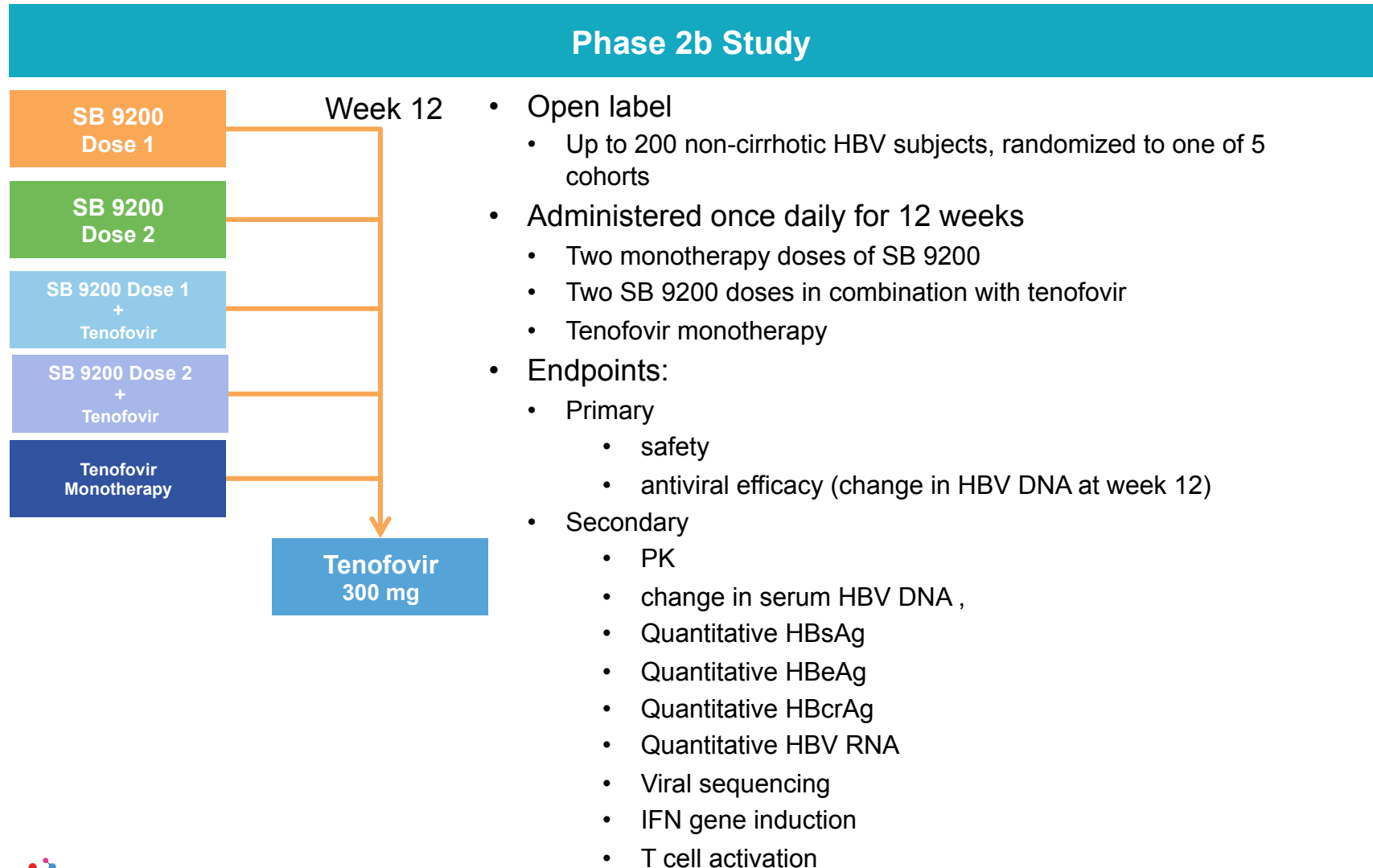
*Clinical trial collaboration with Gilead to evaluate SB 9200 with nucleotide analog Viread*



- Randomized, placebo-controlled, multiple ascending dose trial
  - Up to 100 non-cirrhotic HBV subjects, randomized 4:1 between SB 9200 and placebo
- SB 9200 administered once daily for 12 weeks
  - Following treatment with SB 9200, all patients will switch to 12 weeks of treatment with tenofovir
- Endpoints:
  - Primary
    - safety
    - antiviral efficacy (change in HBV DNA at week 12)
  - Secondary
    - PK
    - change in serum HBV DNA ,
    - Quantitative HBsAg
    - Quantitative HBeAg
    - Quantitative HBcrAg
    - Quantitative HBV RNA
    - Viral sequencing
    - IFN gene induction
    - T cell activation

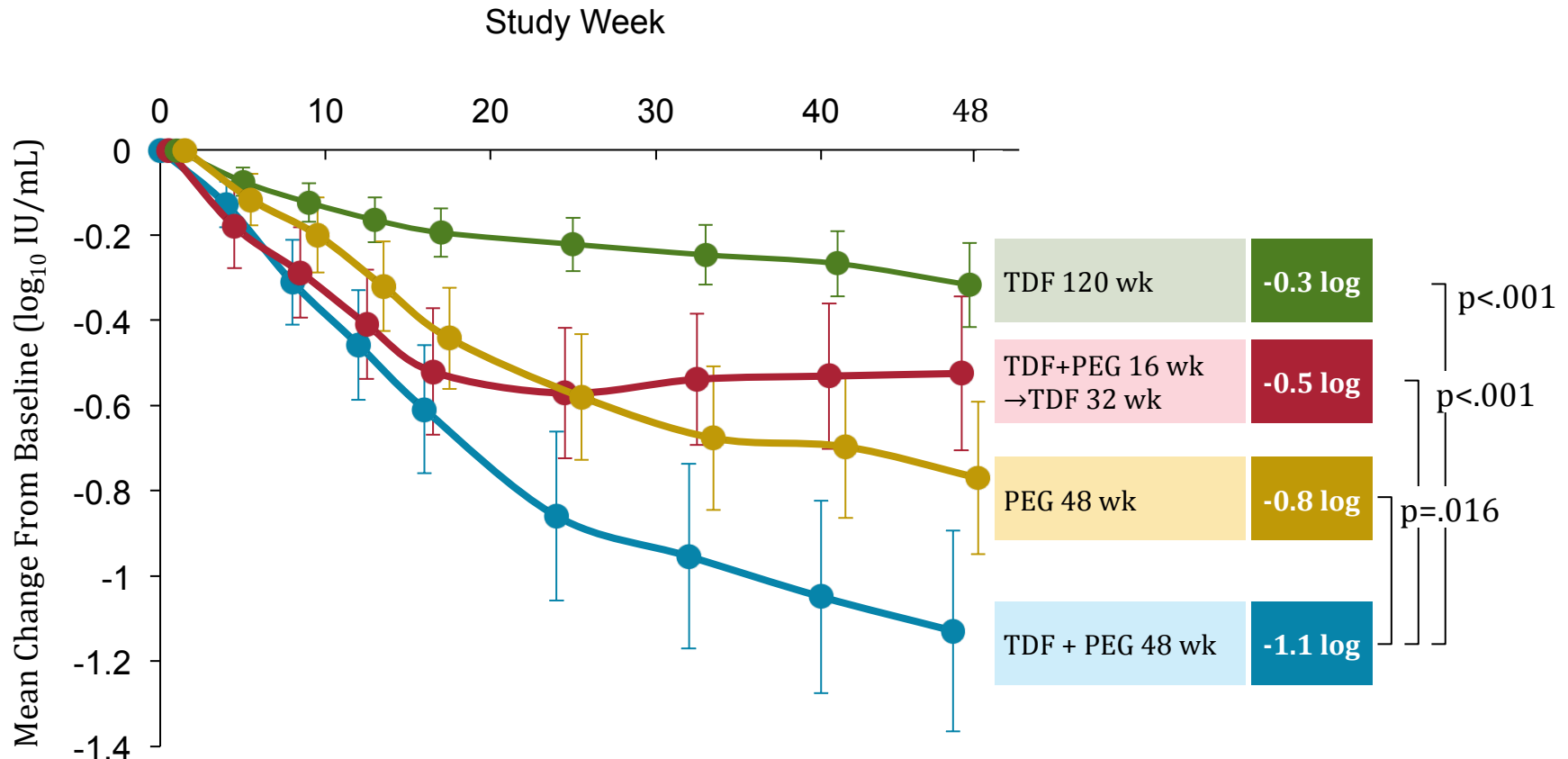
- Initiated in June 2016
  - 10 patients on drug
  - 5 in screening

# Phase 2 ACHIEVE Clinical Study of SB 9200 in HBV – Part B



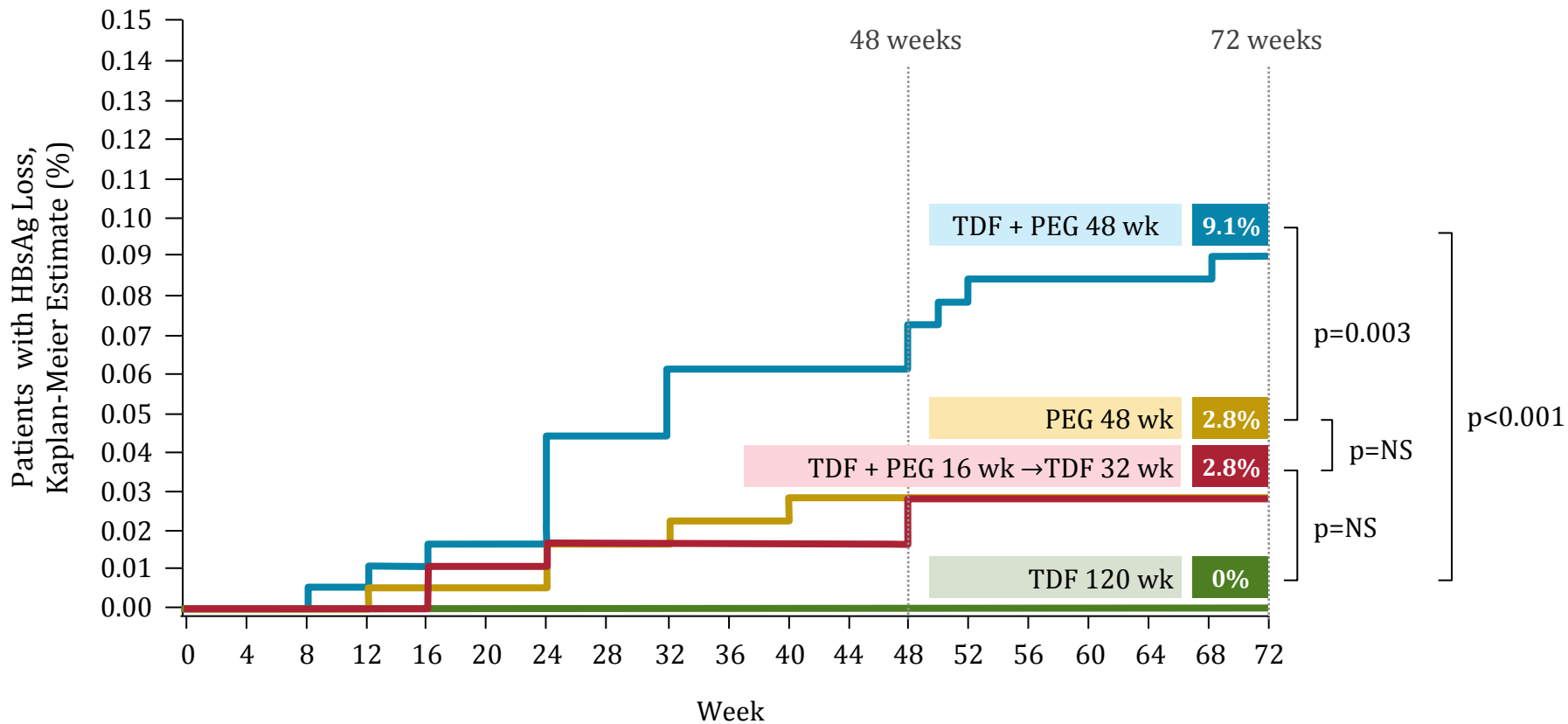
# Results: Change in Serum HBsAg Levels

## On-Treatment Decline in HBsAg Levels at Week 48



3 patients who were re-treated at Week 48 were excluded from Week 48 calculations

# Results: HBsAg Loss Over Time (Week 72)



## On-Treatment Predictors of HBsAg Loss at Week 72

	Univariate p-value	Multivariate p-value	Hazard Ratio*
HBsAg decrease >1 log <sub>10</sub> IU/mL by Week 12	<0.001	<0.001	17.8
HBsAg <100 IU/mL at Week 12	<0.001		
HBsAg <1000 IU/mL at Week 12	<0.001		
HBsAb >10 mIU/mL at Week 12	0.138	0.003	9.97
HBV DNA <15 IU/mL at Week 12	0.014	0.070	15.68
ALT >400 U/L (males) or >300 U/L (females) during first 12 weeks	<0.001	0.031	2.85

\*Multivariate

# Spring Bank and Arrowhead Collaboration for HBV

*Triple combo of SB 9200, ARC-520 and DAA to be evaluated in MONARCH Phase 2b Study*



## Collaboration Highlights

- Innovative clinical study which will evaluate two novel, investigational agents focused on the treatment of chronic HBV
- The collaboration will evaluate SB 9200's oral immunomodulatory characteristics with ARC-520's HBV gene silencing capabilities in delivering a function cure for chronic HBV
- First phase of the collaboration includes conducting preclinical studies with both agents in combination
- Second phase of the collaboration will evaluate the combination of SB 9200 and ARC-520 in a cohort to be added to Arrowhead's ongoing MONARCH Phase 2b study
  - All patients enrolled in the cohort will receive a dosing regimen that includes the triple regimen of SB 9200, ARC-520 and an oral direct-acting antiviral (DAA)

***Potential to demonstrate increased HBV functional cure rates with more favorable tolerability profile and shorter duration of treatment relative to current IFN-based regimens***